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SYMPOSIUM ON DIABETES

THE TREATMENT OF DIABETES WITH DIET AND INSULIN*

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DIET

THE basis of the successful treatment of diabetes is a carefully planned diet adequate in all respects. It is not enough to make provision for the proper amount of carbohydrate, protein, fat and calories; further care is necessary to be sure that an ample supply of vitamins and minerals is included. The best approach to the prescription of any special diet is that of viewing it as a modification of the ideal normal diet so arranged as to promote optimal health. Because the diabetic patient must follow his special diet for years, ample opportunity is afforded for dietary deficiencies to develop, if this possibility is not kept in mind. These can, and must, be avoided by careful planning at the very start of treatment.

Those unaccustomed to the prescription of special diets are often inclined to regard the procedure as complicated. This need not be so. The diabetic diet can be simplified and made easy enough for any patient to understand and follow. The modern diabetic diet allows the average patient fresh fruit, cereal, an egg, one half to one slice of toast, butter and cream for breakfast, and at lunch and supper an average serving of meat, fish, eggs or cheese, liberal amounts of the green, leafy, so-called "5 per cent" vegetables, an average serving of any one of the so-called "10 per cent" vegetables, one half to one slice of bread, perhaps a small potato, butter, and an average serving of fresh fruit. Add to this, tea or coffee, with cream if desired, and at least one half pint of milk for adults and one pint for children, together with a light lunch at bedtime, and one has a simple, easily obtainable, palatable, satisfying diet, furnishing 140 to 160 gm. of carbohydrate, 60 to 80 gm. of protein, 70 to 100 gm. of fat and 1400 to 1900 calories a day. Naturally modifications of this average diet must be made, depending on the age, sex, weight, activity and complicating conditions of the patient, but if a very few basic food values are learned, substitutions, additions and subtractions may be accomplished easily by doctor or patient.

Although the prescription of the diabetic diet can and should be made simple, this should not be done by the use of blanket forms, since such a practice leads to haphazard and slipshod treatment. Dietary therapy must be individualized. An obese patient requires a diet low in fat and in calories, and a lean one the opposite. Growing children require relatively greater allowances of protein, lime salts and calories than adults do, and the diet must be adjusted so as to provide these. It is possible at times to control the hyperglycemia and glycosuria of a diabetic child and still treat him miserably; and because of adherence to the adult type of diets, which may be relatively lower in protein and calories, growth may not take place and dwarfism may result.

Dietary directions must be stated simply and at the same time specifically. Merely to hand the patient a sheet on which are listed "foods forbidden" and "foods allowed" will usually fail to get the best results, unless the diabetic condition is quite mild and amenable to only slight restriction of diet. A preliminary period of a few weeks in which the patient weighs his food accurately on gram scales provides invaluable training. The inconvenience may be reduced to a minimum by the use of scales with a movable dial, which makes unnecessary the separate weighing of containers. The weighing of food should be regarded chiefly as a means to an end, rather than an end in itself; the object is to train the eye and hand of the patient so that after a few weeks he may pick

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out with reasonable accuracy the proper portions of food wherever he may be. Occasional return to weighing is desirable to refresh the memory or to become familiar with the amounts of new foods allowable.

It is often said that diabetic diets are expensive because of the necessity for special foods. The truth is that they are only slightly more expensive than average nondiabetic diets, and probably no more costly than nondiabetic diets that are truly well balanced and adequate in all respects. Articles high in carbohydrate, such as bread, potatoes, beans, corn and macaroni, are the cheapest, to be sure, but when they form the basis of a diet, they are apt to make it deficient in certain respects, chiefly in vitamins and minerals. Special foods such as gluten bread, diabetic flour and bran muffins are no longer necessary and represent a needless expense. As a matter of fact, because of its relatively high protein content, gluten bread actually offers little or no advantage over ordinary bread. Almost the only special foods worth considering are the water-packed fruits and vegetables, which permit a varied selection of food at those times of the year when fresh fruit and vegetables may not be available.

All diets should contain enough milk, cream, eggs and cheese to provide an adequate intake of the lime salts — calcium and phosphorus. The daily requirement of calcium is commonly stated to be 0.7 gm. for adults and 1.0 gm. for children. If the calcium requirement is met in the form of foods, the phosphorus intake will almost invariably be adequate also, because of the common association of the two elements. The usual diabetic diet without milk and eggs or their products will often be found to furnish approximately 0.4 gm. calcium a day; approximately 0.1 gm. calcium is contained in 3 eggs and in each of the following: 3 ounces (83 gm.) of milk, 3½ ounces (104 gm.) of 20 per cent cream, 4 ounces (116 gm.) of cottage cheese and ⅓ ounce (11 gm.) of American cheese.

Whole-grain bread and cereals are far superior to white bread and refined cereals in vitamin and mineral content and should be used in whole or in great part. Patients must be taught to eat green, leafy vegetables and fresh fruit, since these foods contain much in the way of essential minerals and vitamins.

Insulin

Although everyone can appreciate the natural reluctance of patients to submit to daily hypodermic injections, physicians render better service if they reverse the usual viewpoint and, instead of advising insulin as a last resort, follow the rule of prescribing insulin in every case, unless a good reason exists for not doing so. A good, general guide is as follows: if, on a diet that is necessary to maintain health, weight and strength, a patient cannot keep sugar free, insulin should unhesitatingly be prescribed in dosage suited to him. Patients must be urged to receive the benefit from as much insulin as they can without developing hypoglycemia or symptoms of overdosage. Almost without exception, every child with diabetes should receive insulin daily from the day of diagnosis.

It helps to assure patients repeatedly that by taking insulin no habit is formed. One must emphasize that the diabetic patient is all the better and none the worse for having taken insulin, and that if, wisely or unwisely, it is later given up, the worst that can happen is that the patient will revert to the condition existing before he began insulin. Actually, many patients with the milder grades of diabetes are able to give up insulin entirely after the condition has been brought under control with energetic treatment.

Whatever is done, patients should not be asked or allowed to take oral preparations in place of insulin. So far, no effective, practicable oral preparation of insulin has been developed. Despite this, patients are all too often allowed or even advised to take these worthless yet expensive products, if one can accept as reliable the statements made by manufacturing concerns of the amount of their products used annually.

The insulin of choice at the present time is the protamine zinc variety. With many patients, one dose of this type of insulin in the morning before breakfast suffices to bring about satisfactory control of the diabetic condition throughout the twenty-four-hour period. However, with children and young adults and in older patients with more severe diabetes, it is necessary to combine with the turbid, slowly acting protamine zinc insulin a dose of rapidly acting, clear insulin taken at the same time in the morning before breakfast. This clear insulin may be of either the so-called "regular" or the crystalline type. Since June, 1939, we have used successfully the crystalline type of insulin almost exclusively in situations in which a rapidly acting variety was indicated. The division of the total dose of insulin between the clear and turbid types has not only the advantage of better control of diabetes but also of preventing night reactions from an overdose of protamine zinc insulin.

When both types of insulin are taken in the morning before breakfast, we prefer to give them by separate injections, administering the clear in-

sulin first. Some clinicians have permitted the mixing of two types in one syringe, thus making necessary only one puncture of the skin. This has two disadvantages. In the first place, manufacturers place in protamine zinc insulin an excess of protamine; when regular or crystalline insulin is mixed with protamine zinc insulin, a part of the clear type is bound by the protamine so that, depending on the duration of contact between the two types, to a greater or less and probably to a variable degree, one has a slightly larger dose of protamine zinc and a slightly smaller dose of clear insulin than one planned at the outset. Of even more importance is the fact that it is technically difficult to withdraw into one syringe accurately a dose of two types of insulin from two different vials. On the basis of careful studies of the blood-sugar response, Wauchope[1] has likewise concluded that better results are obtained if the two types of insulin are given by separate injections.

When the two kinds of insulin are taken daily in the morning before breakfast, the adjustment of the insulin dosage becomes very simple. Two tests of urine for sugar are important: the test of urine voided before breakfast (preferably not an overnight specimen but a second specimen passed a few minutes later but still before insulin and breakfast), which indicates the effect of the protamine zinc insulin taken the day before; the test of urine voided just before the noon meal, which indicates the effect of the crystalline insulin taken on the same day. With the average patient, these two tests, if carried out by Benedict's method, should give reactions varying between a blue and a light green. Increases or decreases of two units at a time may be made in either or both types of insulin as the urine tests dictate. It is usually best to allow two or three days between changes.

There are certain misconceptions prevalent regarding the use of insulin. Among these may be mentioned the fear of using insulin in the presence of coronary heart disease. In such patients, insulin should be used without hesitation to control the diabetic condition, although with sufficient caution and care to avoid hypoglycemic reactions. A second error is the very prevalent assumption that during times of acute illness, insulin should be omitted when the patient is not eating. This single point has caused untold difficulty for diabetic patients. Repeatedly, patients have been admitted to the hospital in diabetic coma that has resulted from the omission of insulin during an acute infection accompanied by gastrointestinal symptoms, which prevented eating the usual amount of food. Patients forget that, particularly if the diabetic condition is severe, a certain amount of insulin is necessary daily, even though no food is eaten; this becomes all the more important if an infection with fever is present. The patient must be instructed over and over again never to omit insulin during an acute illness, unless the urine is found at three or four hourly intervals to be free from sugar. A third erroneous belief is that in certain patients "insulin does not work." In reporting deaths of diabetic patients, statements are sometimes made that insulin was entirely ineffective in lowering the blood sugar, despite the giving of large amounts, at times several hundred units, within a few hours. The fact is that in certain conditions, particularly acidosis, coma and those rare cases of so-called "insulin resistance," the relative effectiveness of a unit of insulin drops markedly, so that one must discard the usual rules of action and give larger and larger amounts until the desired effect on the blood sugar is obtained. This may mean, as in certain of our patients, approximately 2000 units a day for as long as ten days, but it has been our experience that insulin can never be said to be ineffective, provided large amounts are given early enough.

It has recently been stated that if a diabetic patient is given protamine zinc insulin daily and is kept free from symptoms characteristic of the disease, and if the urine is kept free from acetone bodies, glycosuria and hyperglycemia may be disregarded, even though they may be marked.[2] We enthusiastically approve of the use of protamine zinc insulin, but we believe firmly that it should be used in such dosage, with or without an appropriate dose of crystalline insulin and a restricted diet, that glycosuria is completely or nearly abolished, and the blood sugar kept at a level not far above normal. We believe in the early, vigorous treatment of diabetes and the careful, continuous control of the condition in an attempt to restore normal conditions in the body so far as possible; this conviction has been strengthened by the results of studies in animals reported recently by Haist, Campbell and Best[3] and by Lukens and Dohan.[4] We believe that anyone who follows his patients over years of time until death, and who compares the results in those treated poorly and those treated well, will come to the conclusion that the careful treatment of diabetes pays. Patients may appear to be well for months and years despite constant glycosuria and hyperglycemia, but our experience leads us to believe that these abnormal conditions in the end prove harmful to the patient. Try as we may, it is usually impossible to achieve ideal control of the diabetic condition, but that should be the aim of treatment in every case.

Less than 100 per cent control is a situation to be tolerated rather than to be sought. With such care, one may reasonably hope that most diabetic patients may happily and usefully live out a life expectancy approaching closely that of the normal person, meanwhile avoiding complications characteristic of the disease.

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DIABETES IN YOUTH*

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DURING the last few years, clinical, genetic and physiologic research has done much to clarify and change our concept of diabetes, and this discussion is an attempt to correlate this newer knowledge with the cause, prevention and treatment of diabetes and its complications in childhood, and the cause, prevention and treatment of the common accidents occurring when diabetes complicates pregnancy.

The management of diabetes in the young patient arouses general interest, in spite of the fact that the incidence is certainly not more than 1 in 2500 children under fifteen years of age; however, the complications are sufficiently manifold to bring these patients into all branches of medical and surgical practice.

A brief discussion of the fundamental cause and its mechanism of action is of value, because these are the bases on which serious attempts at alleviation of both experimental and clinical diabetes are being made.

That the tendency to develop diabetes is inherited cannot be doubted. It is the one link connecting all age groups. In childhood, when the expanse of life permits it, family histories of the disease increase with duration. Only 20 per cent of children in our clinic have a known diabetic relative when first seen, but after they have been followed for fifteen years 50 per cent have a known heredity.

The actual evidence in favor of the theory of inheritance of the diabetic tendency lies in the demonstration of diabetes in similar twins, the statistically significant excess of diabetic incidence in the close blood relatives of diabetic as compared with those of nondiabetic patients, and the demonstration of Mendelian ratios of the recessive type in a large series of cases selected at random and in presumably latent diabetic patients.

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Diabetes, even in the child, is not evident at birth or soon thereafter but appears to follow a rhythmic age behavior stimulated at pubescence and at senescence. Of recent years its occurrence has been attributed to complex endocrinal factors — especially an interrelation of the pituitary gland and the pancreas.

At the onset of the disease the child presents presumptive evidence of hyperactivity of the pituitary gland: his height, metabolism and bone and dental development are in advance of the normal for his chronological age, and his puberty is precipitated.

The final production of diabetes by injection of anterior pituitary extract has led to attempts at alleviation by pituitary inhibition. Radiation and extirpation are obviously too dangerous. Estrogens and androgens theoretically capable of depressing pituitary activity have been tried, the former with some success.[1]

Low-carbohydrate diets and hyperinsulinization of the patient at onset have also been attempted, the former in our clinic prior to the discovery of insulin and up to the last decade. Hyperinsulinization was seriously attempted in childhood diabetes in 1930, by Brush[2] in New York City, and for the same purpose perfect control of diabetes is being attempted by Jackson, Boyd and Smith[3] today. Cures have not been reported from any of the attempts. The latent rather than the out-and-out diabetic person must be sought for these experiments, but control of the spread of the disease may be sought by out-breeding, that is, by advising against the intermarriage of families with diabetes.

The treatment of diabetes in children consists in regulation of diet, administration of insulin, adjustment of exercise, education of the entire family and protection of the child against himself.

The caloric requirement, though dependent on surface area, follows age closely in childhood. For simplicity we prescribe calories by age: 1000 at

age one and 100 per year of age until the completion of growth and development. Carbohydrate, protein and fat are prescribed in gram ratios of 2:1:1 respectively.

Insulin is administered to all diabetic children, preferably continuously from the day of recognition of the disease. Few children, only 10 per cent, do well with protamine zinc insulin alone, and 90 per cent require both the rapidly and slowly acting types. The initial prescription for a newly contracted case, which for the time being will do well with protamine zinc insulin alone, is based on age — under five, 10 units, between five and ten, 20 units, and between ten and fifteen, 30 units. The readjustment of the long-standing case is facilitated by continuing with the usual dose of rapidly acting insulin before breakfast, and supplementing with twice that quantity of protamine zinc insulin. Readjustments are then made in accordance with premeal and retiring specimens of urine.

The chemical standards for control are glycosuria of less than 10 per cent of the carbohydrate intake, a normal blood-sugar level before meals and a blood-cholesterol level below 230 mg. per 100 cc.

Postmeal exercise and premeal rest periods are advocated. To the parents one must emphasize the fact that diabetes is not a bed or chair disease but an exercise disease. Education of the entire family, equal to that which is rapidly acquired by the child, cannot be overemphasized. The acceptance of a child's statement relative to diabetic facts as a substitute for more accurate knowledge that has been acquired by the family through self-education leads to tragedy for the child and unsatisfactory care of the diabetes. To provide constructive protection against the child's feeling of security in spite of indiscretions, it has been necessary to start educational units in camps and schools.

Controllable and seemingly uncontrollable complications occur during the course of diabetes in the young patient. Coma, infections, hepatomegaly, some of the skin complications and failures of growth and development are now correctable. The degenerative and deficiency diseases remain unsolved, but, I believe, are not unsolvable. These complications I shall merely catalog, and thus summarize their essential differences in behavior and their management when they occur in childhood rather than in adult life.

Excess of incidence, simplicity of treatment and sureness of favorable prognosis characterize coma in the young population. The severity of the disease in the child, as well as the occurrence of irregularities of diet, the omission of insulin and infections, account for the relatively high incidence. The treatment consists largely of three measures — insulin, fluids and gastric lavage. The prognosis for recovery, unless the patient has a lethal infection or is actually moribund before treatment is inaugurated, is 100 per cent.

The decreased incidence of tuberculosis in the entire population is reflected in the juvenile diabetic population. Chemotherapy protects the adolescents from deaths from septicemia, which formerly so often followed infections of the skin and urinary tract.

Hepatomegaly, of interest physiologically and of importance clinically because of the bouts of abdominal pain, is corrected and prevented by protamine zinc insulin. One biopsied case in our series showed 10 per cent fat and 12 per cent glycogen in the liver.

Metabolic skin lesions are seen frequently in the child. Xanthosis, due to the excessive intake and failure of metabolism of carotene, is corrected when the foods high in carotene are eliminated. The lesions of xanthoma diabeticorum, which we have not seen in a patient treated with protamine zinc insulin, disappear when the blood fat falls to normal levels. The early lesions of necrobiosis lipoidica diabeticorum — perhaps cutaneous gangrene — have been controlled by x-ray therapy, but no satisfactory treatment of the late lesions has been found.

Neuritis seldom occurs in childhood, but is not uncommon in patients in their twenties. It has not been controlled with vitamin B therapy. Diabetic nocturnal diarrhea, commoner in the young patient and frequently an accompaniment of neuritis, appears to have been controlled by liver extract.

The incidence of degenerative complications in juvenile diabetes far exceeds expectation. Cataracts occur early in its course, are not always progressive, and can be treated surgically. Retinal hemorrhages may be reversible. Retinitis may also be reversible but, unfortunately, the incidence of its severest form — retinitis proliferans — is high in long-standing severe diabetes.

Based on an analysis of diabetic children who have had the disease for fifteen years, arteriosclerosis appears inevitable. The lesion can be attacked from different angles. If it results from uncontrolled diabetes, hyperglycemia, acidosis or dehydration, the more perfect control of the diabetes by combined insulin therapy should prevent it in the future. If it is due to improper metabolism of fat, lipotropic substances, such as choline and lipocaic, may prevent its occurrence. Even though it may prove to be a degenerative stigma inherited with diabetes, arteriosclerosis should yield to some therapeutic agent, just as

diabetes is controlled by insulin. If, as seems possible, it is a part of the complex endocrine imbalance, more perfect and combined endocrine therapy may solve the difficulty as it appears to have done in the next two problems, namely, failures of growth and development, and accidents of pregnancy in diabetes.

The situation of pseudodwarfism in diabetes appears paradoxical. The failure of growth is not observed until several years after onset. Obesity occurs in proportion to the duration of retarded growth, and the child has the characteristics of pituitary failure — delayed development of bone and of teeth, with normal intelligence. Three possible explanations are that it is a congenital anomaly, the result of undernutrition or the result of fatigue of the pituitary gland. Along with failure of growth, mildness of diabetes usually occurs. These patients respond to intramuscular anterior pituitary extract and oral thyroid therapy. The increased severity of the diabetes is sacrificed for the social and economic importance of the problem.

A mechanism similar to that responsible for the production of diabetic pseudodwarfism appears to explain the high incidence of accidents when pregnancy complicates diabetes. These data are more convincing because, although we have not measured the hormones in the dwarfish patients, we have measured the hormones of our pregnant diabetic women.

Our present conception of the mechanism of the accidents in diabetic pregnancies has been the outcome, first, of the realization that insulin therapy did not lower fetal mortality (preinsulin 42 and insulin 38 per cent) and, secondly, of the behavior of diabetic pregnancies in relation to the pregnancy hormones, which Smith and Smith[4] first studied in a number of our patients, to extend their work on pre-eclamptic toxemia.

Our present conception is that an abnormal rise of serum chorionic gonadotropin after the twentieth week predicts accidents, that the accidents are caused by failure of production or metabolism of estrin and progestin, and that they are prevented by continuous substitutional estrin and progestin therapy in replacement doses.

This statement is based on a series of 84 cases of completed pregnancies studied between 1936 and 1941. The early analyses were made by Smith and Smith as part of their research, the later ones in the laboratory of the New England Deaconess Hospital, where we have attempted to establish them on a routine rather than a research basis.

Classified by prolan values, the rise occurring two to six weeks before clinical signs, there were 36 patients with normal behavior. There was no toxemia, no premature deliveries, and three neonatal deaths, — due to asphyxia pallida, hemorrhagic disease of the newborn and multiple congenital anomalies, — making fetal survival 92 per cent.

Twelve patients with significant rises had no treatment. All the mothers had an abnormal course, 9 of the 12 had pre-eclamptic toxemia, 3 had premature deliveries, and fetal survival was 42 per cent. The clinical picture was clarified. Maternal and fetal behavior fell into two classes. Either the mother developed a lightninglike toxemia, usually with hydramnios, and delivered a macerated stillborn child, or without toxemia she delivered prematurely a large atelectatic infant dying within a few hours of birth.

The next step was an attempt at prevention. At the suggestion of Smith and Smith, estrin and progestin* in doses as near replacement as possible were given continuously after the rise of the prolan. Signs of toxemia were controlled. Premature deliveries did not occur, and fetal survival was 13 out of 14 cases, or 93 per cent, contrasted with 42 per cent in the untreated group.

Although this therapy appeared to be successful, because of the cost it was a physiologic curiosity. For this reason, at the New England Deaconess Hospital we substituted synthetic and inexpensive preparations, Stilboestrol† and Pranone. Eleven cases were treated with oral substitutes. There were two fetal deaths, including one due to erythroblastosis. Another 11 abnormal cases were treated with intramuscular Stilboestrol and Proluton. Ten of these infants survived. The fetal survivals in the three groups are as follows: normal prolan, 93 per cent; high prolan, untreated, 42 per cent; and high prolan, treated, 89 per cent.

The characteristics that occur in the infant are gigantism and hyperplasia of the islands of Langerhans, which we correlate with the imbalance of pregnancy hormones. In the experimental animals prolan has also produced both these conditions.

Congenital anomalies, usually not fatal, are a manifestation of the hereditary nature of diabetes. Diabetic patients themselves have similar anomalies. Hypoglycemia, not a fatal accident, occurs in most newborn infants.

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Thus the outlook for diabetes in the young patient today is good. Duration of life is assured. Progress in prevention and control of complications is advancing. In two periods of life the diabetic patient, like the experimental diabetic animal, shows definite evidence of hormonal in-

*Progynon and Proluton were partly supplied through the courtesy of the Schering Corporation, Bloomfield, New Jersey.

†The Stilboestrol was supplied through the courtesy of E. R. Squibb and Sons, Company, New York City.

terrelation. In the animal this relation appears most marked among the pituitary gland, pancreas and adrenal glands, but in the clinical diabetic patient, when growth and development and pregnancy complicate the disease, an interrelation of gonads, pancreas and pituitary glands is most marked.

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DIABETIC HAZARDS*

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PERSONS with sugar in their urines run many hazards. The first is that of being diagnosed a diabetic when the disease is nonexistent. Approximately one seventh of all the patients we have seen with sugar in the urine were thought by us not to have had diabetes at the first visit. One must not be careless with this group. Such patients should have their urines examined every three months for life, warned against overweight and cautioned to report to their physicians if any unusual symptoms occur. In the early days, when blood-sugar tests were not available, 10 per cent of these cases developed diabetes, but more recently the percentage has dropped to 6; it is barely possible that with the more accurate interpretation of glucose-tolerance tests the number of persons who from the experience of the past would later develop diabetes will be still further curtailed, because they will be proved to have had the disease originally.

The glucose-tolerance test itself is a hazard if the patient's diet has previously been restricted in carbohydrate. Such patients, whether or not they have ever shown sugar in the urine, may give a positive reaction to the test. I need not amplify this statement, but simply re-emphasize the necessity of learning from the patients whether they actually have been restricting their carbohydrate before putting them through this procedure. One such case occurred some months ago. A patient with glycosuria came for diagnosis. Sugar was found in the urine, and he was given a glucose-tolerance test. It indicated that he had diabetes, because the blood-sugar level rose above 170 mg. per 100 cc. during the test, and glucose was present in the specimens obtained. Knowing that his diet had been restricted, I advised him to live on a free diet during the continuance of his vacation and to return in ten days. This he did. A repetition of the test showed the urine to be perfectly normal.

Another diagnostic hazard is the failure to discriminate between pentose or fructose and glucose. We have had 9 such cases. One of these, a child four and a half years of age, had been given insulin for two years. When he arrived for treatment, despite his trip of 1000 miles, the blood sugar was normal. It continued normal for a day or two despite a slight upper respiratory infection. It is true that sugar was present in the urine. However, the technicians followed the established rule that whenever a new patient comes for treatment, pentose must be excluded if the Benedict test is positive. This is very simply done. One performs the Benedict test in the ordinary way, but sets up a duplicate without heat and keeps the mixture of urine and Benedict's solution at room temperature until the following morning. If pentose is present, the Benedict's solution will be reduced even without heat, but of course this will not take place with glucose. Such a reduction of Benedict's solution in the cold also occurs with levulose. You can imagine, therefore, my gratification in being able to tell the parents of the child that diabetes did not exist and that a special diet and insulin were unnecessary. All our cases, and apparently all such cases thus far recorded have occurred in Jews; the origin of those traced by Lasker[1] has been in what was formerly Poland.

An identification card should be in the pocket of every diabetic patient. It is true that with protamine zinc insulin, reactions are less common than heretofore, but they may occur and the patients must not take any chances. On the reverse side of the identification card that we give our patients are rules for the differential diagnosis of an insulin reaction and diabetic coma. To drive home the desirability of an identification card, I was told of a patient far away from New England who was

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put in jail; the disease was unrecognized, and death followed. A happier, although somewhat embarrassing result occurred with one of my diabetic clergymen. He was candidating for a church in a new locality, but when he reached the town, woke up to find that he was in jail instead of in the pulpit. Perhaps his life was saved by an identification card or the mute witness of a couple of lumps of sugar in his pocket.

Living alone is truly a diabetic hazard. Each patient should have a close friend. A diabetic patient who has a diabetic twin is fortunate. My diabetic girls are so bright that they sometimes marry doctors, and my diabetic boys so intelligent that they deplete the ranks of the nurses at the New England Deaconess Hospital. Perhaps I should not say so much about the danger of living alone, but I have known of such a method of life resulting in dire catastrophes.

Diabetes should be acknowledged by those who have it. It is not a disease to be ashamed of unless one has been informed that he or she is hereditarily disposed and yet has become fat. One in four of all the people in the country has a diabetic relative. A good share of those who have diabetes could not have prevented it, even if they had avoided obesity, because they were born with a diabetic heredity. If the presence of diabetes is more generally admitted by intelligent patients, people will become more and more accustomed to it and will assume, just as they properly should, that diabetic patients can get along very well and be of service to themselves and others. Meanwhile their friends will allow ther to be protected. Diabetic patients often undergo social embarrassments needlessly. Thus they may have taken their insulin, but the expected meal thereafter may be delayed, and a reaction may ensue. Although this is less frequent with protamine zinc insulin than formerly when, with regular or crystalline insulin, injections were made several times a day, reactions do occur. The diabetic woman may be very energetic in preparing the food at a church strawberry festival, and so busy that she forgets the lengthening interval that has occurred between the dose of insulin and the beginning of the meal; a reaction may take place, to the confusion of all concerned. If the disease had been less concealed, the hostess or a friend might have shared in preventing the delay in eating.

Unusual exercise promotes the tendency to a reaction. With regular insulin or crystalline insulin one takes a little extra carbohydrate at the first sign of a reaction, but patients employing protamine zinc insulin will do better if they eat their extra quota of carbohydrate at the beginning of the exercise.

Gastrointestinal upsets often are the precursors of a reaction. During such episodes, patients should always take some carbohydrate at frequent intervals, electing the form that can be best retained — tea or coffee with sugar, milk and Vichy water, ginger ale or similar preparations.

Automobile driving is a definite hazard. The patient should make it a rule never to drive an automobile unless carbohydrate has been taken within two hours. Of course it is safer for him to have a companion in the car, and that is another reason for not living alone. On the other hand, I wish to state emphatically that I have known diabetic patients who made a practice of driving thousands of miles a year in their daily work and yet never got into trouble. These persons, however, are most reliable. I confess that at one time I knew of a diabetic woman who drove a school bus. It always worried me, but I never had a more reliable patient. She never drove without taking food a very short time before driving, and now that she has given up driving on account of age I can say that she never had an accident; in fact, once when there was an emergency on account of trouble with the automobile, she mastered it. One of my very best patients has been an aviator, but fortunately he is now married and has given up acting as a pilot.

The differential diagnosis of diabetic coma and an insulin reaction is often difficult. I cannot blame the doctor who does not have an opportunity to see many diabetic patients if he fails in such a diagnosis. That is why we ask all our patients to carry an identification card with the points in diagnosis on the reverse side. I have known tragic examples of failure in such a diagnosis. Aside from the standard points of differential diagnosis, what should be done? Recourse must be had to a laboratory.

Laboratories are lifesaving in diabetes because through them the doctor can intelligently treat a patient with an insulin reaction or diabetic coma. Each doctor and each patient should always know where blood-sugar tests and tests for acidosis, including the carbon dioxide content or combining power of the blood plasma, can be performed promptly, not only by day but by night, on Sundays and on holidays. Laboratories cost only about $200. No town should be without a laboratory in which a blood-sugar test can be done. Doctors must co-operate more and more to make this possible. In one town in Maine there is a diabetic child whose doctor taught the young nurse attendant how to do a blood-sugar test. She has done

tests for years, once a week, for the child. She does tests for the patients of other doctors, and when a case of diabetic coma came to the fourteen-bed hospital in the town, she was the one called on to clinch the diagnosis by estimating the sugar in the blood. I hope that some of my diabetic girls can be trained to be technicians, because then they will demonstrate their usefulness to the communities in which they live.

The omission of the routine test of the urine is dangerous in diabetes. I always dread to have a patient give up testing because for a time he has found his urine constantly sugar free. Of course some patients can rightly do this. The ordinary patient, however, should test the urine daily. Over and over again the rule has been relaxed only to find later that the diet has also been relaxed. Thousands of useless tests are better than the failure to recognize the return of active diabetes with or even without the development of diabetic coma.

A double diagnosis should always be considered in diabetes. A single diagnosis to explain all the symptoms that a patient manifests was the rule we were all taught to adopt in our early medical education. Such a rule, however, is fallacious in diabetes, and double diagnoses are now more frequent. I took off my hat to a young physician, who came to work with us after graduating from the Peter Bent Brigham Hospital, when he diagnosed cerebrospinal meningitis in the presence of an attack of diabetic coma and with prompt, intelligently applied and efficient treatment saved the patient's life. Over and over again this rule holds in diabetic coma. The patient in diabetic coma seldom dies, unless there is an additional diagnosis such as appendicitis, cholelithiasis, pyelitis, paranephric, ischiorectal or vulval abscess, coronary thrombosis, uremia, apoplexy or pneumonia. It is safe to assume, when a diabetic patient is not doing well, if his diet is adjusted and if he is taking the usual dose of insulin, that another diagnosis exists; one should always look for the accompanying diagnosis.

Errors in measuring insulin are common. Regardless of whether the patient is a doctor, lawyer or a minister, whether he is a patient who has taken insulin for a week or for ten years, it is possible for such errors to occur. Therefore, it is a good rule always to ask to see the syringe that the patient uses, to check up closely both the type of insulin and how he measures and injects it and never to trust to his story if in any way the diabetes is not being properly controlled when one thinks that it should yield to treatment. To guard against errors in measuring insulin, our group believes that the simplest type syringe, namely, a 1-cc. syringe divided into tenths, is the best. I considered myself fortunate to be able to tell a doctor, who was health officer of a large city, that his uncomfortable feelings during the latter part of the morning were not due to his circulation, but to the fact that he was taking 60 units of insulin when he thought he was taking 30 units.

Insulin should never be omitted when sugar is present in the urine. The mere fact that a patient is not eating is no reason to omit a dose of insulin. Omit insulin only when the urine is sugar free. Of course, one always checks up the statement that sugar is or is not present in the urine. It may have been secreted from the kidney into the bladder at 2 a.m. and consequently found in the urine when the bladder is emptied at 7 a.m., thus giving rise to the patient's wrong impression that the urine secreted at that particular moment shows sugar. A second specimen test a few minutes later will clear up the situation, provided that the bladder has been thoroughly emptied at the previous voiding. Any patient who improves so much that he can be told that insulin can be omitted must be doubly cautioned to test his urine more frequently in the future than ever before to be sure that the sugar does not return. Unless the doctor does this, he is likely to be embarrassed at a future visit of the patient or by an emergency summons.

Failure to recognize that diabetes can improve and grow milder is a definite hazard. It is almost as serious as failure to recognize that it can grow worse. In one case the failure may lead to an insulin reaction, and in the other to diabetic coma. There are so many mild diabetic patients today who do improve, and such a considerable percentage who by living faithful dietetic lives and taking proper exercise could give up their insulin safely, that it is a shame not to recognize their improvement and enable them to do so.

Toes are a greater hazard than teeth. A diabetic patient can have a toothache, and he will fly to the dentist to have it treated or taken out. But if he has a toe ache, most likely he will neglect it or eventually go to the doctor, who may dress it instead of taking it off. If these patients could only get rid of their toes as easily as they get rid of their teeth, how fortunate they would be. Other lesions of the feet arise in diabetes, resulting in gangrene, but most of the troubles in the feet begin in the toes. Never let a diabetic patient go through a visit in your office unless he takes off his shoes and stockings. This is sometimes a sad and disagreeable procedure for the doctor, but if the feet are always examined, they will be cleaner and cleaner at each subsequent visit, and the time may come when you will be able to trust the removal of one instead of two stockings, although that is a very

risky procedure. I do not dare to look up how much of the free-bed money for diabetic patients in the New England Deaconess Hospital is spent on neglected toes, but I venture to say that the charity money devoted to the toes of elderly patients is five times that expended on diabetic patients in their teens. Consider the difference in the efficiency and expectation of life of the two groups.

A defeatist policy will never win a diabetic war. Always attack diabetes aggressively — the more aggression, the younger the diabetic and the more recent the onset of the disease. Best[2] has shown that diabetes can be prevented in a dog following the injection of anterior pituitary extract, provided insulin is simultaneously administered. Indeed, if a dog is fasting it is impossible to give it diabetes by the injection of anterior pituitary extract. Lukens[3] has shown in a cat that even after two months the diabetes definitely produced by injections of anterior pituitary extract can be cured by energetic treatment with insulin. In the cat, for some months following the development of the disease, the islands of Langerhans in the pancreas are in the stage of hydropic degeneration, and in that stage the lesions are reversible and the diabetes can be cured.

How thankful I am that the words "prevention" and "cure" have now entered the vocabulary associated with diabetes, even though they apply alone to experimental diabetes in an animal. There is no question in my mind that some of those who hear me today will live to see the extension of these experiments to diabetes in man.

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THE TREATMENT OF PNEUMOCOCCAL PNEUMONIA*

With Special Reference to the Use of Sulfathiazole, Intramuscular Serum, the Francis Test and Histaminase

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THE specific therapy of pneumococcal infections has been undergoing changes so rapidly in recent years that careful evaluation of the various types of therapy has been impossible, with the result that there are many uncertainties and differences of opinion concerning relative merits. It is the purpose of the present communication to report experiences with 80 cases of pneumococcal pneumonia that were treated at the Peter Bent Brigham Hospital between October, 1939, and June, 1940.

Detailed statistical analysis of a series of cases of this size is not worth while. The type incidence was not unusual; all but a single case fell into one of the 32 pneumococcal types of Cooper. The average age of our patients, forty-nine years, is considerably above that usually reported. Bacteremia was found in only 10 cases. The gross mortality rate in a small series of cases is not of much significance, since it depends considerably on chance. With the extremely effective agents now available, mortality is rare in adequately treated cases unless the pneumonia is complicated by some other serious debilitating condition, such as heart disease, cancer or chronic alcoholism, or is far advanced when therapy is begun. A brief survey of the 9 fatalities in the present series bears this out.

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Case Reports

CASE 1. G. B. (No. 57025), a 70-year-old man, was admitted after several days' illness — the exact duration was uncertain. The blood culture contained many Type 9 pneumococci, estimated at 60,000 per cubic centimeter. The leukocyte count was 5200. Three lobes were involved. The patient was treated with sulfathiazole, concentrated rabbit serum intravenously and blood transfusions (1200 cc.). He died 36 hours after admission. Blood culture just before death showed less than 1 colony per cubic centimeter. Autopsy showed dense consolidation of three lobes, massive empyema, and purulent arthritis of one sternoclavicular joint.

CASE 2. M. D. (No. 57187), a 60-year-old woman and a chronic alcoholic, was admitted in coma, with multiple bruises and a fractured clavicle, following a fall during a drinking spree. The patient was unconscious for 30 hours. On the 4th hospital day, signs of pneumonia (Type 8) developed in two lobes; the patient succumbed 40 hours later. She was treated with sulfathiazole, and concentrated horse serum intramuscularly. Autopsy was not permitted.

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CASE 3. A. W. (No. S62399), was a 51-year-old woman. Since childhood she had had rheumatic heart disease involving the mitral and aortic valves, and had been decompensated previously. Operation, consisting of closure of colostomy following resection of colon for regional ileitis, was performed. The patient developed signs of pneumonia (Type 14) in two lobes on the first postoperative day, and was treated with sulfapyridine and with concentrated rabbit serum intravenously. The response was excellent; the temperature fell to normal and the signs of pneumonia cleared rapidly. On the 8th postoperative day, the patient went into collapse and died rather suddenly. Autopsy showed that the pneumonia was practically gone, but there was a large fresh mycotic aneurysm on a mitral-valve leaflet.

CASE 4. J. F. (No. 57224), a 68-year-old man with a Type 8 infection, was admitted and gave a history of failing health, with insidious onset of respiratory infection followed by pneumonia during two weeks previous to entry. He was found to have lymphatic leukemia, with generalized lymph-node enlargement and splenomegaly; the leukocyte count was 400,000 to 600,000. There were signs of pneumonia in two lobes. The patient was treated with sulfapyridine and concentrated horse serum intramuscularly. There was no response to treatment. The condition steadily became worse, and the patient died on the 7th hospital day, having been stuporous for 3 days. Permission for an autopsy was not obtained.

CASE 5. P. D. (No. 56391), a 45-year-old man with a Type 5 infection, had been followed in the outpatient clinic for many years because of chronic cough, dyspnea and asthma. Previous x-ray and physical examinations had shown marked enlargement of the right side of the heart — cor pulmonale. The patient was admitted to the hospital, gravely ill, on the 4th day of pneumonia and showed extreme cyanosis and dyspnea. He was treated with oxygen and sulfapyridine. He died 5 hours after admission. No autopsy was performed.

CASE 6. C. M. (No. 57214), a 67-year-old man with a Type 3 infection, was admitted on the 6th day of pneumonia. Blood culture on admission contained 50 colonies of Type 3 pneumococci per cubic centimeter. The leukocyte count was 4200. Three lobes were involved. Chest aspiration yielded a small quantity of pus, either from empyema or from a lung abscess. The patient was treated with sulfathiazole, sulfapyridine and concentrated rabbit serum intravenously. He died on the 2nd hospital day. No autopsy was performed.

CASE 7. J. H. (No. 56503), a 73-year-old woman with a Type 3 infection, was admitted on the 7th day of disease; two lobes were involved. There was an old history of hypertension. The patient was treated with sulfathiazole and concentrated rabbit serum intravenously, with no response other than a fall in temperature, and died 55 hours after admission. No autopsy was performed.

CASE 8. C. D. (No. 56309), a 73-year-old man with a Type 4 infection, was admitted with a history of poor health for several weeks; he had been vomiting for 2 or 3 days before admission. He was extremely dehydrated. Examination revealed consolidation of the entire right lung. The patient was treated with sulfapyridine for several days, with no obvious effect on the pulmonary disease. The temperature remained normal throughout his stay in the hospital. On the 14th day his pulse suddenly became rapid and weak, and he died within a few hours. Autopsy showed an unresolved pneumonia in the right lung, estimated by the pathologist to be of at least 6 weeks' duration. Death probably was due to recent perforation of a gastric ulcer. Incidental findings were carcinoma in the cecum and in the prostate.

CASE 9. G. L. (No. 56837), a 45-year-old man with a Type 3 infection, was admitted on the 5th day of pneumonia with a history of chronic alcoholism. Two lobes were consolidated. The leukocyte count was 1200. The blood culture was positive — 50 colonies per cubic centimeter. The patient was treated with sulfapyridine. He showed evidence of peripheral vascular collapse on admission, and died within less than 24 hours. Autopsy showed lobar pneumonia (right middle lobe), bronchopneumonia (left upper lobe), atelectasis of the rest of the lungs, bilateral hydrothorax, fibrinous pericarditis, cholelithiasis and hepatomegaly.

The chemotherapeutic agents used in these cases were sulfapyridine and sulfathiazole.* The antipneumococcus serums were chiefly those supplied by the Commonwealth of Massachusetts (concentrated horse serum for Types 1, 2, 5, 7 and 8 and commercial concentrated rabbit serum for Types 4, 9, 14 and 18). Commercial rabbit serums of other types were also available for seriously ill patients. Two patients were treated with a Type 3 concentrated rabbit serum.†

The general plan of treatment was to administer either sulfapyridine or sulfathiazole to all patients, and in addition to give serum to all patients with types of pneumonia for which serum was available. This routine use of serum is at variance with the practice of some authorities,[1, 2] who advocate treatment with drugs alone, resorting to serum only in certain types of cases, such as those not responding to the drug in twenty-four to thirty-six hours and those with bacteremia, renal calculi and so forth. Our reasons for employing serum routinely in addition to the sulfonamides were as follows: there is good evidence, both experimental and clinical, that a combination of chemotherapy and antiserum is more effective against pneumococcal infections than is therapy with either one alone; by giving serum in addition to sulfapyridine, the dosage of the drug can be reduced considerably; it is reasonable to suppose that the less drug that has to be given, the less danger of toxicity; also patients who are not receiving sulfonamides eat better and have a more rapid convalescence.

In these cases the average total dose of sulfapyridine when used alone was 17.8 gm., as compared with 10.2 in patients treated also with serum. For sulfathiazole the respective averages were: 31.2 and 16.7 gm. When both chemotherapy and

*The sulfathiazole and sodium sulfathiazole were supplied through the courtesy of the Squibb Institute for Medical Research, New York City.

†Supplied through the courtesy of the Squibb Institute for Medical Research, New York City.

serotherapy were employed, the plan generally followed was to give sulfapyridine or sulfathiazole as soon as the diagnosis of pneumonia was made. After six to twelve hours of drug therapy, treatment with serum was instituted. The reason for this spacing of therapy was to allow time for absorption of the drug and the attainment of a therapeutic blood level, and to allow for the lag period that probably exists before the bacteriostatic effect of the sulfonamide compound begins to take effect.[3, 4] Then an attempt was made to bring about a critical termination of the infection with serum. As soon as this occurred, all therapy — drug and serum — was stopped. Thus in many cases no therapy was given after the first ten or twelve hours, as is shown by the following typical case.

Case 10. L. K. (No. 56546), a 51-year-old man with a pneumococcal infection Type 3 and a negative blood culture, was admitted on the second day with involvement of the right upper lobe. Sulfathiazole was begun two hours after admission. A Francis test was negative. Concentrated rabbit serum (150,000 units) was given intravenously 8 hours after admission. Three hours later the Francis test was still negative, and therefore 50,000 units of serum was administered intravenously. Two hours later the Francis test was strongly positive. All therapy was stopped, and the pulse fell from 150 to 95, followed by a more gradual drop in temperature. The total dosage of sulfathiazole was 10 gm. The convalescence was rapid and uneventful.

Comparison of Results with Sulfapyridine and Sulfathiazole

Sulfapyridine has been in general use since the fall of 1938, whereas sulfathiazole, a sulfonamide derivative that is similar to sulfapyridine in its range of antibacterial action, has just been released for general use. Very little has yet been reported as to clinical experience with sulfathiazole in large series of cases. Flippin, Schwartz and Rose[2] recently reported a comparison of results in 100 patients treated with sulfapyridine and 100 treated with sulfathiazole. They considered the effects of the two drugs to be about the same. In a report to the Council on Pharmacy and Chemistry of the American Medical Association, Long[5] states that early experience indicates that sulfathiazole is about as effective as sulfapyridine in the treatment of pneumococcal pneumonia.

We have treated 37 pneumonia patients with sulfathiazole, alone or in combination with serum. Naturally, no positive conclusion can be drawn from this experience. There was no response to sulfathiazole in 3 patients in whom the administration of sulfapyridine brought about a favorable termination of the infection. It is possible that there may be similar sulfapyridine-resistant cases that will respond to sulfathiazole, but we have not seen them; we are therefore inclined to believe that sulfapyridine is slightly more effective.

There are unmistakable differences between the two compounds. Sulfathiazole is more rapidly absorbed and excreted in the urine,[6] and to obtain satisfactory blood concentrations it is therefore necessary to give larger doses. For that reason, the schedule of dosage followed in most of our cases was 3.0 or 4.0 gm. initially, followed by 1.5 gm. every four hours. The blood concentrations achieved tended to vary, much as they do with sulfapyridine, from 1.5 to 15.0 mg. per 100 cc., and equally good therapeutic responses were obtained at different levels. Determination of free sulfathiazole gives an accurate index of the amount present in the body fluids, because very little is conjugated, whereas some patients on sulfapyridine may have a total blood concentration of 10 mg. with a free level of only 2 mg. per 100 cc. Since the conjugated compounds are very insoluble in the urine and much less effective therapeutically, this lack of conjugation is an advantage.

Sulfathiazole has one decided superiority over sulfapyridine in that it is much less apt to cause nausea and vomiting. Almost none of the headache, dizziness, delirium and general malaise that so commonly accompany sulfanilamide administration are seen with sulfathiazole, and cyanosis is minimal. Among approximately 50 patients who have been given sulfathiazole for various infections, we have seen no patients with blood destruction or agranulocytosis, although more cases must be treated to get valid information on this point.

On the other hand, there are two toxic manifestations that we have observed even in our small series. Two women receiving sulfathiazole developed on the extremities skin eruptions that resembled erythema nodosum, although the lesions were not tender. One of them had a conjunctivitis associated with a burning sensation and photophobia. This type of skin rash and conjunctivitis has been described by Haviland and Long.[7] The most serious toxic reaction we have encountered involved the kidneys and was characterized by a marked diminution in urine output, associated with albuminuria and, in one case, with many granular casts. In a series of 50 cases of various infections treated with sulfathiazole this reaction has occurred four times in 3 patients. One patient was tried on sulfathiazole twice, and each time his urinary output decreased steadily over a period of forty-eight hours, despite a generous fluid intake. Neither sulfanilamide nor sulfapyridine had this effect. In no case did gross or microscopic hematuria or pain, as reported by Arnett,[8] give any

warning of the danger, but careful check on the output of urine showed that it was rapidly diminishing, and examination of the urine showed albumin. In these patients, the condition cleared fairly promptly when sulfathiazole was discontinued and fluids were forced in large amounts, but high concentrations of sulfathiazole were excreted for the next few days, often enough to precipitate as a yellow dust from the urine, with crystals visible in the sediment. These crystals under the microscope look like radially striated balls or dumb-bells or like sheaves of sticks. It seems conclusive that fluids should be given in liberal amounts during sulfathiazole therapy, and that a careful check must be maintained on the output of urine. This is particularly true when sodium sulfathiazole is given intravenously to achieve rapidly a high blood concentration. We have without mishap used single intravenous injections of 4 gm. of sodium sulfathiazole in distilled water, given slowly as a 5 or 10 per cent solution, in several patients at the start of therapy. Our limited experience with sulfathiazole seems to be in entire agreement with the larger experience of Long and his associates.[9]

One point noted by Flippin, Schwartz and Rose,[2] which was also true in our cases, is that sulfapyridine appears to bring the temperature down more rapidly than sulfathiazole. We believe, however, that the effect on the temperature may not be a reliable index of the antibacterial action of the two drugs, since we have evidence, experimental and clinical, indicating that sulfapyridine has an antipyretic action.[10] Consequently, a more rapid drop in temperature does not necessarily mean a more effective antibacterial action.

There is little agreement as yet as to the length of time chemotherapy should be continued in the treatment of pneumonia. Long and Wood[11] advised continuation of therapy with sulfapyridine (in diminishing doses) until the patient is ready to leave his bed. They stated that there is considerable danger of relapse if therapy is discontinued too soon. Fox, Rosi and Winters[12] urged that sulfapyridine therapy be continued until agglutinins can be demonstrated in the blood, and they reported demonstration of agglutinins in every one of 50 patients studied. On the other hand, there is evidence that demonstrable free antibody is not essential to recovery from pneumococcal pneumonia. Francis and Tillett[13] studied patients who recovered from pneumonia without any specific treatment, and reported that in some of them no excess of antibody could be demonstrated. Spring, Lowell and Finland,[14] recently reported inability to demonstrate type-specific agglutinins in the blood of some of their sulfapyridine-treated patients during recovery. Kneeland and Mulliken[15] found precipitins in the blood of only 4 of 19 sulfapyridine-treated cases of pneumonia during the recovery phase. Our policy has been to discontinue drug therapy comparatively early. The average duration of therapy in our cases treated with drug alone was 3.6 days for sulfapyridine and 4.0 days for sulfathiazole. In many of these cases, presence of antibodies in the circulation could not be demonstrated by the Francis test at the time therapy was discontinued. Yet in only one case was it necessary to readminister sulfapyridine because of further activity of infection. Early discontinuance of the drug has the advantage of relieving nausea and improving the appetite of most patients, and of decreasing the likelihood of other more serious toxic effects.

Intramuscular Serotherapy

Intramuscular administration of serum has been employed successfully in diphtheria for many years, but has been used little in pneumonia. We believe that the intramuscular route of administration has one great advantage that is worthy of consideration: it practically never causes a chill or a thermal reaction. The disadvantage of intramuscular administration is, of course, the fact that absorption of antibody into the circulation is slow, which probably renders this route of administration considerably less effective than the intravenous one when serum alone is employed. However, antibody can be administered by this route fairly satisfactorily, as illustrated by the following case.

Case 11. J. B. (No. 57216), a 43-year-old man with a Type 1 pneumonia and a history of arrested pulmonary tuberculosis, duodenal ulcer and renal calculi, was admitted on the 3rd day of his disease; one lobe was involved. Blood culture was negative. Because of the presence of renal calculi, it was decided to treat the pneumonia with serum alone. The Francis test was negative. Three hours after admission, the patient was given 60,000 units of concentrated horse serum intramuscularly. Thirteen hours later, the Francis test was still negative, and he was given 150,000 units of serum intramuscularly. Ten hours after the second injection, the Francis test was found to have become positive. Three hours later the temperature was normal. Recovery thereafter was uneventful, and the patient left the hospital on the 11th day.

Finland and Brown[16] studied the absorption of antipneumococcus antibody after intramuscular administration and were able to find antibody in the circulation as early as two hours after administration; the peak of absorption occurred twenty-four to forty-eight hours later. We have administered serum intramuscularly in conjunction with chemotherapy in 20 cases, and have found the results to be satisfactory in most cases. The amounts of serum given at one time varied from 60,000 to 150,000 units. Most of the serums that were given

intramuscularly were known to cause chills when given intravenously, and doses of this size would almost certainly have caused severe thermal reactions if given by the intravenous route; yet there was not a single chill or rise in temperature in this series of cases. Effective absorption of antibody was demonstrated in most cases by the development of a positive Francis test. It should be emphasized that the intramuscular route is not the ideal one, but may be used to advantage with serums apt to give chills or in patients in whom thermal reactions would be dangerous. The dosage may have to be considerably larger, and we have had a few patients in whom the absorption of horse serum so administered was unsatisfactory. However, in severely ill patients, after chemotherapy has been started, a large dose of serum may be given intramuscularly and later be supplemented with smaller doses of intravenous serum.

The Francis Test

The Francis test is a valuable guide in the determination of serum dosage,[17–19] and is performed by injecting 0.1 cc. of a 1:10,000 solution of type-specific pneumococcal capsular polysaccharide intradermally. A positive reaction presumably indicates the presence of free antibody in the circulation. It appears in eight to fifteen minutes and is a typical immediate reaction, with erythema and wheal and pseudopodia formation. The advantage of this test is that it tells one within a few minutes whether or not a patient has an adequate supply of antibody. Thus it is a much more rapid, and in many cases, more accurate indication than a fall in body temperature. Although its main usefulness is in guiding serum dosage, the test may also be used in cases treated with sulfonamides alone, since it becomes positive when the natural antibody makes its appearance. Its greatest drawback is the occurrence of false positive reactions in some persons — some patients show a typical immediate skin reaction to the injection of a pneumococcal polysaccharide, although they have no antibody for that type of pneumococcus. In such a person, it would be thought that sufficient serum had been given after the first test. This danger can be eliminated, however, by testing all patients prior to serum therapy. In those who react positively, the Francis test cannot be used.

In the present series of cases the Francis test was used in 42 patients, and in 4 of these a false positive reaction was encountered. In addition, 3 patients never developed a positive reaction at times when there was good evidence that an excess of antibody was present. In the remaining 35 patients the Francis test was a reliable and useful guide.

In regard to the false negative Francis test, that is, failure to react in spite of the presence of excess of antibody in the circulation, it should be pointed out that the skin must possess the capacity to develop a reaction. Some gravely ill patients lack this capacity. One method of testing for it is to inject 0.1 mg. of histamine (0.1 cc. of a 1:1000 solution of histamine phosphate) into the skin. Failure to react to histamine with erythema and a wheal shows that the skin lacks the ability to give a positive Francis test, and one should be so guided.

Details concerning the use of the Francis test. Once the type of the pneumococcus has been determined from examination of the sputum or blood culture, 1 cc. of a 1:10,000 dilution of the capsular polysaccharide* of this type is withdrawn into a syringe; if the solution is 1:1000, 0.1 cc. is drawn into a syringe containing 0.9 cc. of sterile saline. A single test dose, 0.1 cc., containing 0.01 mg. of polysaccharide, is injected into the skin of the flexor surface of the forearm; 0.1 cc. of sterile saline may be injected in another site to control the patient's reaction to the trauma of injection. If this initial test gives a positive wheal reaction in fifteen minutes or less, it cannot be used as a guide to serum dosage. If the reaction is negative, as it is in most cases, the test can be used as a guide to therapy, and the syringe containing the polysaccharide dilution should be kept at the bedside.

One hour after each intravenous dose of serum the patient should be retested, and if the reaction remains negative, more serum should be given. As soon as a definitely positive reaction is obtained, no more serum need be administered. If the temperature falls, but then rises again, the patient should be retested. If the test has become negative, more serum should be given; if it remains positive, the temperature is not due to a relapse, but to empyema, infection with another type of organism or some other complication, and no more serum of this type is needed. Fever of 101 or 102°F. frequently occurs on the first or second day following serum administration.

If large doses of serum are given and the test remains negative, 0.1 mg. of histamine should be injected intradermally. If this produces no wheal and erythema, it can be concluded that the patient is too ill to give a positive skin reaction to any form of irritation, and the test will not be valid until the patient's condition improves.

It must be emphasized that the test depends on accurate bacteriologic work. If the sputum is wrongly typed, the test means nothing, since the polysaccharide injected is not that of the actual in-

*Solutions of the specific capsular polysaccharides are now commercially available.

fecting type. One should always remember that mixed infections with two pneumococcal types or with pneumococci and hemolytic streptococci may occur, that laboratories are fallible and that if a patient's course is unsatisfactory, another sputum typing and blood culture are indicated.

The practical utility of the Francis test is illustrated by the following case:

CASE 12. A. W. (No. 56518), a 41-year-old man with a Type I pneumonia, was admitted on the 1st day of disease. One lobe was involved. Blood culture was negative. Therapy with sulfathiazole was begun one hour after admission. The Francis test was negative. Twelve hours later, 60,000 units of concentrated horse serum was injected intramuscularly. Nine hours later the Francis test was still negative, and 60,000 units of serum was injected intramuscularly. Four hours later the Francis test was still negative, and a third dose of 60,000 units of serum was therefore given intramuscularly. Four hours later the Francis test was strongly positive. All therapy, drug and serum, was discontinued. The temperature fell to normal during the next ten hours, but on the next day it rose to 102°F. The Francis test was repeated, and was found to be still strongly positive. With the evidence of excess antibody present in the circulation, it was considered unnecessary to administer more sulfathiazole or serum. This proved correct, since the temperature again fell to normal. The patient's convalescence was impeded by the occurrence of serum sickness, after which he made a good recovery and was discharged on the 24th day.

HISTAMINASE FOR THE PREVENTION OF SERUM SICKNESS

Foshay and Hagebusch[20] recently reported encouraging results in the treatment of serum sickness by the use of histaminase. We were unable to confirm this in the present series of cases. Histaminase* was given both orally and intramuscularly, in doses equal to or greater than those used by Foshay and Hagebusch. The plan followed was to begin therapy with histaminase on the fifth day following serum administration, and continue it through the tenth day. In the event of development of serum sickness, histaminase therapy was continued until symptoms subsided. As shown in Table 1, there is no evidence that in our cases histaminase had any effect in preventing serum sickness. Its incidence in treated cases happened to be slightly greater than in those patients who did not receive histaminase.

TABLE 1. *Prophylactic Use of Histaminase for Serum Sickness.*

PATIENT	AGE yr.	TYPE	AMOUNT OF SERUM units	HISTAMINASE units	SERUM SICKNESS
C. R.	47	1	240,000 i.m.	1, b.i.d., i.m.	None
R. C.	34	1	60,000 i.m.	1, b.i.d., i.m.	None
B. F.	30	1	60,000 i.v. 120,000 i.m.	1, b.i.d., i.m.	None
A. deM.	59	1	150,000 i.m.	2, b.i.d., i.m.	None
L. S.	13	1	90,000 i.m.	1, b.i.d., i.m.	Fever 4 days; arthralgia 3 days; urticaria 1 day.
M. W.	66	1	70,000 i.v. 90,000 i.m.	2, b.i.d., i.m.	Fever 3 days; arthralgia 3 days; urticaria 3 days.
I. M.	57	14	100,000 i.v.	75, daily, orally	None
D. MacK.	58	5	135,000 i.m.	75, daily, orally	None
E. G.	43	4	120,000 i.v.	75, daily, orally	None
C. C.	55	1	150,000 i.m.	75, daily, orally	None
H. McG.	19	1	120,000 i.m.	45, daily, orally	None
D. C.	72	8	80,000 i.m.	45, daily, orally	Fever 1 day
J. C.	72	8	40,000 i.v.	45, daily, orally	Fever 3 days
A. W.	41	1	180,000 i.m.	45, daily, orally	Fever 3 days; arthralgia 5 days; urticaria 4 days.
A. M.	37	1	30,000 i.v. 90,000 i.m.	45, daily, orally	Arthralgia 3 days
C. M.	63	6	70,000 i.v.	None	None
J. B.	43	1	210,000 i.m.	None	None
F. S.	37	8	240,000 i.m.	None	Fever 2 days; arthralgia 3 days; urticaria 2 days.
S. E.	49	2	200,000 i.m.	None	None
L. K.	50	3	100,000 i.v.	None	None
V. V.	45	1	60,000 i.m.	None	None
D. N.	54	1	270,000 i.m.	None	None
K. F.	45	3	50,000 i.v.	None	None
V. F.	24	5	40,000 i.v. 80,000 i.m.	None	None
F. L.	86	8	60,000 i.m.	None	Fever 1 day
J. C.	17	5	120,000 i.v.	None	Fever 2 days; arthralgia 2 days; urticaria 1 day.

CONCLUSIONS

Experiences in the chemotherapy and serotherapy of pneumonia are reviewed.

Sulfathiazole is comparable to sulfapyridine in

*Histaminase (Torantil) was supplied through the courtesy of the Department of Medical Research, Winthrop Chemical Company, New York City.

its effectiveness against pneumococcal pneumonia. It has the advantage of causing less nausea than sulfapyridine. The urinary output must be carefully watched during its administration, since suppression of urine was the commonest toxic manifestation encountered.

In the majority of cases it is not necessary to continue chemotherapy until the time when liberation of antibodies is expected to take place. Relapse seldom occurs if therapy is discontinued after three to four days.

The combined use of chemotherapy and serotherapy is recommended as the most satisfactory form of treatment in severe pneumonia.

Intramuscular administration of serum has the advantage of avoiding thermal reactions, and in conjunction with chemotherapy it appears to be a practical procedure in many cases.

The Francis test properly controlled is a valuable aid in the estimation of serum dosage.

Histaminase has not been found to have any action in preventing the occurrence of serum sickness.

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PAIN ASSOCIATED WITH RENAL APLASIA*

Report of Two Cases

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DURING the past year on the Urological Service of the Massachusetts General Hospital we have encountered two rather interesting and unusual cases of pain associated with congenital aplasia of the kidney.

Case Reports

CASE 1. A 14-year-old girl was first seen in the Emergency Ward on July 26, 1939, complaining of frequent episodes of cramplike, right-sided abdominal pain of 6 weeks' duration. The pain was occasionally associated with epistaxis, headache, anorexia and malaise. Two days before admission, the attacks became more frequent, and the pain assumed a sharp, lancinating character, radiating to the right lower quadrant. There was slight burning and frequency on micturition, and nocturia thrice. Pain was aggravated by walking, running and stooping, and was somewhat alleviated by pressure over the tender area in the right upper quadrant.

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Physical examination revealed moderate right costovertebral tenderness and diffuse tenderness in the right flank and right upper quadrant. Urinalysis was negative. The leukocyte count was 10,000, the blood pressure 116/65. The nonprotein nitrogen of the blood serum was 17 mg. per 100 cc. The temperature, pulse and respirations were normal. An intravenous pyelogram revealed a hypertrophic, normally functioning left kidney that was incompletely rotated (Fig. 1). No kidney was visible on the right, and there was no excretion of dye on that side. Cystoscopy showed a normal bladder and normal ureteral orifices. The right ureter was catheterized, and obstruction encountered 24 cm. from the bladder. Skiodan was injected and failed to reveal a kidney on that side, the dye returning down the ureter. It was thought that the patient probably had a cut-off aplastic right kidney, but that this was not responsible for her pain.

The patient was discharged and returned six weeks later with a story of recurrent attacks of pain. Physical and laboratory findings were unchanged. Extensive studies were carried out, including a gastrointestinal series, barium enema, Graham test and psychiatric and orthopedic consultations, all of which revealed no evidence of disease. The x-ray films were reviewed, and it was

believed that the patient's symptoms might be due to the presence of a horseshoe kidney with a cut-off right segment. Because other evidence of disease was lacking, it was decided to explore the right kidney.

At operation, what appeared to be a normal ureter was

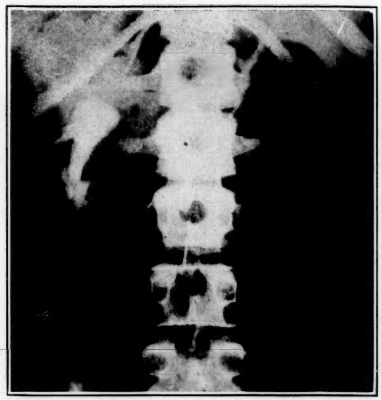

FIGURE 1.

observed. When freed up, this was found to be under tension and to degenerate into a fibrous cord attached above to a rounded body, 8 cm. in length, that consisted of a mass of smooth cysts filled with clear fluid. There was a definite artery running to the mass from the region of the aorta. This was tied and cut, and the cystic body, with the ureter as far as the pelvic brim, removed. The pathological report described an irregular mass of fat and fibrous tissue measuring 8 by 4 by 2 cm.; the mass contained numerous gray, smooth, transparent cysts measuring up to 3 cm. in diameter and containing a clear, straw-colored fluid. On section the cut surface presented a firm gray fibrous appearance, with no normal kidney tissue.

The microscopic report was as follows:

> Scattered through a dense fibrous-tissue stroma, there are large and small tubular structures, some slightly papillary, lined by a layer of cuboidal epithelium; in many places these have smooth muscle walls. These tubules are very probably remnants of the Wolffian ducts. There are also many smaller tubules, some filled with pink-staining casts, which are very similar to the colloid-filled tubules seen in chronic pyelonephritis. No definite glomeruli are identified. The stroma in places is very vascular (Fig. 2).

Convalescence was uneventful. The patient was discharged in good condition on the 11th postoperative day. She has been followed in the Out Patient Department for 3 months and is entirely asymptomatic so far as her former complaints are concerned. She is in excellent general health.

CASE 2. A 25-year-old store clerk was admitted to the Urological Service of the Massachusetts General Hospital because of pain in the left back of 2 years' duration. The pain was dull and aching and was localized to the left costovertebral region. It was exaggerated by bending forward and was almost constantly present.

Physical examination was entirely negative except for moderate left costovertebral tenderness. A gastrointestinal series done 9 months before admission was reported negative. On excretory pyelography, there was prompt excretion of the intravenous dye from the right side, filling a slightly dilated pelvis and ureter (Fig. 3). There was a very questionable kidney shadow on the left, with no excretion of the dye on that side in 60 minutes. Cystoscopy revealed a normal bladder and normal ureteral orifices.

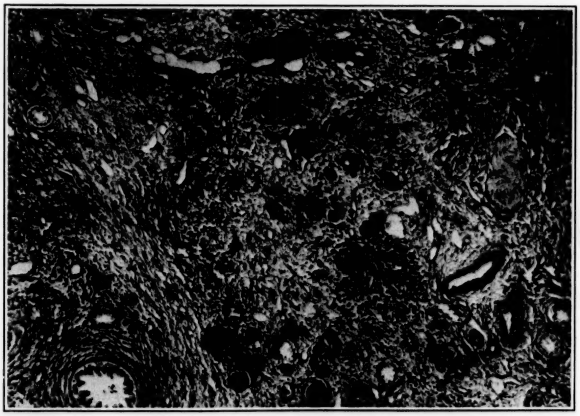

FIGURE 2.

A ureteral catheter engaged in the left orifice but could not be passed farther than 5 cm., and no dye could be injected past this obstruction; a catheter was easily passed to the right kidney, and a normal drip of clear urine ob-

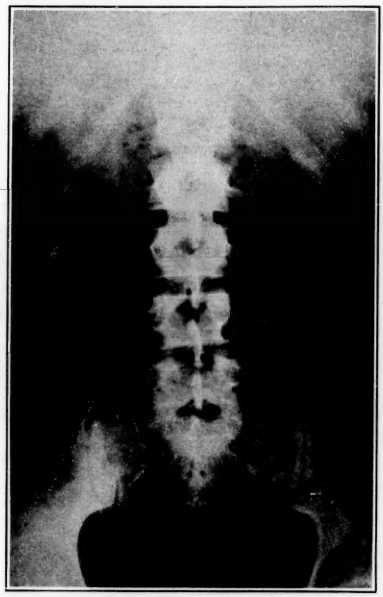

FIGURE 3.

tained (Fig. 4). Since the patient was unable to carry on his work because of the discomfort, it was decided to explore the left renal region on the possibility that the pain was due to an atrophic blocked kidney.

At operation no ureter was seen, but in its place was a fibrous cord that terminated about the level of the 2nd lumbar vertebra. Exploration of the renal fossa revealed a small, flat, brownish body measuring 5 by 4 by 1 cm. and studded with 4 or 5 small purplish cysts. This mass was attached to a fibrous pedicle that contained several small sclerotic vessels. The pedicle was clamped, cut and tied, and the mass removed in toto. What appeared to be a normal adrenal gland was felt above this body. A diagnosis of aplastic kidney was made by the pathologist. Microscopic examination revealed findings similar to those of Case 1. The tubules, however, were much larger and more numerous, and the colloid-filled small tubules less conspicuous; no glomeruli were observed (Fig. 5).

The postoperative course was uneventful. The wound healed by first intention, and the patient was discharged entirely asymptomatic on the 11th postoperative day. At the present time, 5 months after operation, he has had no recurrence of his previous symptoms and is in excellent health.

These two cases exemplify congenital defects or arrest in development of one kidney associated with hypertrophy of its mate. They are differentiated from congenital hypoplasia of the kidney in that at no time have they possessed excretory function. The etiology of the pain in both cases is rather obscure; it may perhaps be explained by the pressure of the cystic bodies on the surrounding tissues, or as in the first case, by tension on the obliterated ureter.

This rare condition has been observed occasionally at post-mortem examination. Campbell[1] reported 39 cases of renal aplasia in a series of 13,000

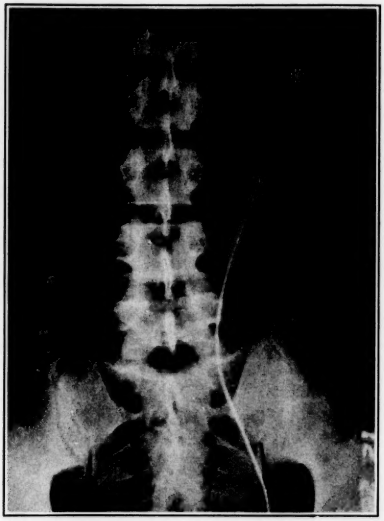

FIGURE 4.

autopsies at Bellevue Hospital and claimed that its incidence is four times that of congenital absence of the kidney.

Clinically this condition is seldom encountered. MacKenzie and Hawthorne[2] reported three cases similar to the above in which excision of a cystic aplastic kidney produced permanent relief of symptoms. Gutierrez,[3] in an interesting discussion of the developmental defects of the kidney, postulates the following conditions in true renal aplasia: no true kidney; no evidence of pelvis; absence of true renal pedicle; renal artery small or absent; ureter incompletely developed and not patent; no excretion of urine; no renal function; bladder with

two normal ureteral orifices or one ectopic ureter; histologic section of the supposed renal mass reveals glomeruli and tubules showing arrest in the development of the renal organ; cystoscopy, catheterization of the ureters and descending or ascending pyelography are necessary for diagnosis of the condition. This author reports two cases of renal aplasia. In one, the preoperative diagnosis was made by observing four small pea-sized shadows in the excretory urogram that gave the impression that the dye had been excreted by some kidney substance, although no definite kidney outline could be seen.

FIGURE 5.

CONCLUSIONS

Abdominal pain in certain rare cases is associated with congenital aplasia of the kidney; surgical intervention results in complete relief of symptoms.

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INTUSSUSCEPTION OF THE JEJUNUM DUE TO CARCINOID TUMOR

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ABOUT 75 per cent of the cases of intussusception occur in children under two years of age,[1] although a specific cause for the production of the invagination in children is usually not found. Perrin and Lindsay[2] found only 18 patients over fourteen years of age in a series of 314 cases collected at the London Hospital from 1903 to 1920.

In adult cases of intussusception, a tumor is the commonest etiologic agent. Eliot and Corscaden,[3] in their analysis of 300 cases of intussusception in adults, found a tumor of the bowel in 40 per cent of the cases, of which the greater number were benign. Other causes were ulceration of the bowel of tuberculous, bacillary or typhoid origin in 14 per cent, and a Meckel's diverticulum in 12 per cent. Among the tumors usually found were polyps, leiomyomas, lipomas, fibromas and carcinomas.

Tumors of the small intestine are relatively infrequent as compared with tumors of the other parts of the gastrointestinal tract. Raiford[4] in 1932, in a very full discussion of tumors of the small intestine, reported a series of 88 cases found among 11,500 autopsies and 45,000 surgical specimens at the Johns Hopkins Hospital. He was also able to collect from the literature 339 tumors of the small intestine that he considered authentic. The 88 cases comprised 8.9 per cent of the total number of gastrointestinal tumors, which was 986. The 50 benign and 38 malignant small intestinal tumors comprised 23.8 per cent and 4.9 per cent respectively of the total benign tumors (210) and total malignant tumors (776) of the gastrointestinal tract. The benign tumors included adenomas, fibromas, myomas, lipomas, angiomas, pancreatic rests, hemangiomas, argentaffin (carcinoid) tumors and cysts. In this series the carcinoid or argentaffin tumors numbered 7, and were all benign.

Tumors of the small intestine often produce no symptoms, and are found only incidentally at autopsy. The symptoms that they do produce are usually the result of obstruction of the intestine, incomplete or complete, or of the production of an intussusception.

Freilich and Coe[5] were able to collect from the literature a total of 3284 cases of intussusception, of which 462 were enteric; and of these, 24 were jejunal. Altogether, from 1852 to 1934, 29 recorded cases of jejunal intussusception occurred in patients from four months to sixty-seven years old, with an average age of 27; 15 cases were in men, 13 in women, and 1 not specified; 18 were of a simple jejunojejunal type, 9 were double jejunal, and 2 were triple jejunal. The majority were caused by such tumors as polyps, lipomas and papillary adenomas. No case of jejunal intussusception due to a carcinoid tumor was listed.

No specific character of the carcinoid tumor, as compared with other tumors, makes it less likely to produce an intussusception. The relative rarity of carcinoid tumors probably accounts for the paucity of such occurrences. In 1930, Cooke[6] collected from the literature 104 cases of carcinoid tumor of the small intestine, and added 11 of his own. Ariel,[7] in the most recent review of the subject, found 111 cases in the literature since 1930, and reported 11 additional cases, thus making the total of reported cases 237.

Among these 237 carcinoid tumors, only 3 cases of intussusception occurred. These were reported by McGlannan and McCleary,[8] Jones[9] and Ariel.[7] In all 3 the tumor was located in the ileum.

Because of the extreme rarity of its occurrence, a recent case of intussusception of the jejunum due to a carcinoid tumor is worth reporting.

Since no new features of pathologic histology appeared in this case, no lengthy description of carcinoid tumors will be given. During the last thirty years, since the name "carcinoid" was given to these tumors by Oberndorfer,[10] a considerable literature has accumulated on the subject. Excellent contributions to and reviews of the problems of pathogenesis have appeared, together with adequate descriptions of the clinical features; for these the reader is referred to the papers of Masson,[11] Forbus,[12] Cooke,[6] Raiford,[13] Bailey,[14] Humphreys[15] and Ariel.[7] The work of Masson, particularly, has thrown light on the origin of these tumors from the Kultschitzky cells in the wall of the crypts of Lieberkuhn and on the relation of these cells to those of the chromaffin system and to the nerve plexuses of the intestinal wall. The demonstration of the identity of the

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silver-staining granules in the cells of these tumors with those in the Kultschitzky cells was chiefly due to the researches of Masson, and the term "argentaffin tumor" as a synonym of carcinoid tumor was therefore introduced.

These yellowish tumors were referred to as carcinoids by Oberndorfer[10] because of their superficial similarity to true carcinoma. They were at first considered to be essentially benign. But as increasing numbers were reported, many cases with unmistakable metastasis were found, as evidenced by extension to the regional lymph nodes, mesenteric fat and liver. In Cooke's[6] series of 115 cases, 21, or 18 per cent, had metastasized. In Ariel's[7] series of 111 reported cases, 33, or 30 per cent, had metastasized, and among his own 11 cases, metastases were found in 5. Thus, metastases occurred in 59, or 25 per cent, of the 237 cases recorded to date.

The decision as to where the line should be drawn between benignity and malignancy in these tumors is a difficult one, except when metastases actually occur. Thus Humphreys[15] states, "The small submucous nodule is certainly a clinically insignificant lesion, and yet it already shows an infiltrative manner of growth which, in a gland cell tumor, is one of the criteria of malignancy." This tendency to invade the muscle and serous layers of the intestinal wall, and to extend out into the mesentery, warrants a diagnosis of carcinoma even in the absence of demonstrable metastases in the lymph nodes or liver. Furthermore, even in the absence of invasive features, the appearance and arrangement of the cells may suggest carcinoma to the experienced pathologist.

In most cases, carcinoid tumors are of slow growth, and are slow to metastasize. This lends a good prognosis to cases that have produced early clinical manifestations, and resection is likely to be followed by favorable results. That the carcinoid tumor is a far from harmless lesion, however, is emphasized by Ariel,[7] who found that of 38 patients with clinical symptoms produced by carcinoid tumors, 14 died as the result of the tumors or their metastasis, or of attempts at extirpation. Of the 38 patients, 13 were subjected to resection, and were well for varying periods.

Resection is the treatment of choice. The value of x-ray therapy has not yet been evaluated, although the recession of a local recurrence in one case led Ariel to believe that these tumors might be radiosensitive.

Case Report

M. B., a 19-year-old girl, was admitted to the Beth Israel Hospital on May 5, 1939. The past history was noncontributory.

About two weeks prior to entry she had had a sudden onset of epigastric colicky pain and vomiting, which continued intermittently for the next 3 days. Enemas afforded temporary relief. Subsequently the patient seemed well until 11 a.m. of the day of admission, when she was again suddenly seized with severe colicky pain in the epigastrium, and to the left of the umbilicus. She vomited 3 times, and complained of persistent nausea. The bowels moved once.

On examination, the patient appeared pale, and in obvious distress from severe pain. The abdomen was not distended, but a rounded fullness was visible just to the left of the umbilicus. Palpation at this site revealed a mass that was rounded in shape, about the size of an orange, tensely elastic, immovable and moderately tender. There was no tenderness elsewhere in the abdomen, and the abdominal wall was generally soft. Pelvic and rectal examinations were negative. The temperature was 98.6°F., the pulse 80, and the blood pressure 134/85.

Examination of the blood showed a red-cell count of 4,340,000, with 90 per cent hemoglobin, and a white-cell count of 13,000, with 85 per cent segmented polymorphonuclears, 5 per cent young polymorphonuclears, 8 per cent lymphocytes and 2 per cent monocytes. The urine was normal. The sedimentation rate was 7 mm. in 45 minutes. Examination of the stools revealed no blood.

The preoperative diagnosis was acute intestinal obstruction, due either to a strangulated paraduodenal hernia or to an intussusception.

Operation was performed about 8 hours after the onset of acute pain. Under spinal anesthesia, a 5-inch left paramedian muscle-splitting incision was made. When the peritoneum was opened, a large sausage-shaped mass of intestine, fully 10 cm. in diameter and over 30 cm. in length, was found occupying the epigastrium and left para-umbilical region; it appeared purplish, and exceedingly tense. The entire mass was delivered from the wound. It was identified as a jejunojejunal intussusception. The terminal portion of the mass abruptly changed to collapsed, narrow jejunum. At the proximal end, the intussuscepted jejunum was markedly constricted, and the accompanying mesentery appeared twisted, edematous and ecchymotic. Reduction of the intussusception was effected after considerable difficulty, rupture of the distended, thinned-out intussuscepted bowel being a constant hazard. After reduction, the intussuscepted bowel was found to be the site of a tumor, readily visible at a constricted, retracted segment of the intestine and showing a depression or umbilication on the serosal surface. Palpation revealed a firm mass, about 5 cm. in diameter. The mesentery proximal to the tumor had accompanied the intussuscepted intestine, and as a result appeared traumatized, ecchymotic and edematous, with some question of the patency of its blood vessels. There were numerous enlarged, but soft, lymph nodes in this portion of the mesentery. No metastases in the liver or omentum could be seen or felt.

The entire intussuscepted length of intestine, including the tumor and the involved mesentery, was resected, altogether about 20 cm. The ends of the divided jejunum, held by Payr clamps, were closed with an inverting suture of chromic catgut and two purse-string sutures of Pagenstecher linen. The two portions of jejunum were then apposed, the closed ends adjacent to each other, and a side-to-side anastomosis made in the usual manner, using chromic catgut for the through-and-through suture, and Pagenstecher linen for the outer serosal suture. The bowel was then returned to the peritoneal cavity,

and the abdominal wound closed in layers, without drainage.

The pathological report by Dr. Alfred Plaut was as follows:

> The resected specimen of the jejunum is 20 cm. long. About 3.5 cm. from the one end, on the antimesenteric side, the lumen is almost occluded by a flat, ovoid, irregular, mushroom-shaped formation, 5.3 by 3.0 by 1.0 cm. [Fig. 1]. Somewhat eccentrically, there is a depression in the center of which a small elevation is situated. The depression measures 1.7 by 1.2 cm.
>
> The surface of the tumor in general is smooth and finely granular, with some brownish material adherent to it. There is one small, ovoid, deep-red elevation at the edge. The mucosa directly outside the tumor appears normal. There is very little thickening of the muscle coat. The mucosa in the remainder of the specimen is hyperemic and edematous. No ulceration or necrosis is seen with the naked eye.
>
> On the outside, corresponding to the tumor, the serosa is partly yellowish, partly cyanotic. There is an irregularly ovoid transverse depression. The serosa has lost its sheen throughout. The cut edge of the tumor is homogeneously grayish (after fixation).
>
> Microscopically, the tumor tissue is entirely necrotic on the surface, and considerably necrotic throughout, so that proper cytological studies cannot be made. The cells are not very closely packed. The stroma contains very few cells except those due to the inflammatory reaction caused by the necrosis. There are few blood vessels.
>
> The tumor is situated chiefly in the submucosa, but the mucosa is widely invaded [Fig. 2]. The muscle coat is partly destroyed by the tumor. In the muscle coat a linear arrangement of the tumor cells is distinct. The cells are medium sized, with large nuclei [Fig. 3]. Many fragments of nuclei are seen in the necrotic areas. None of the lymph nodes contain tumor.
>
> Diagnosis: malignant carcinoid.

FIGURE 1. *Gross Specimen.*

Flat, ovoid, mushroom-shaped tumor occluding the lumen of the jejunum.

The patient's postoperative course was uneventful. She was treated immediately with an indwelling Levine tube, no liquid or food by mouth, continuous intravenous drip of 5 per cent glucose in physiologic saline solution or distilled water, adequate sedation, and sulfanilamide intravenously and by hypodermoclysis. Fluid by mouth was started on the 2nd postoperative day, and sulfanilamide discontinued at the end of the 3rd day, a blood concentration of 5.5 mg. per 100 cc. having been obtained.

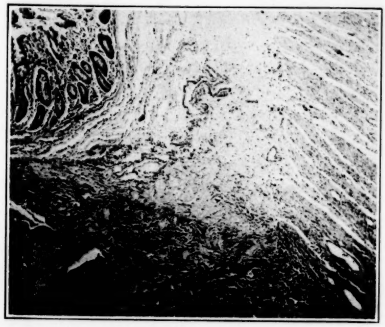

FIGURE 2. *Low-Power Magnification.*

Diffusely growing tumor cells separating the glands of the mucosa.

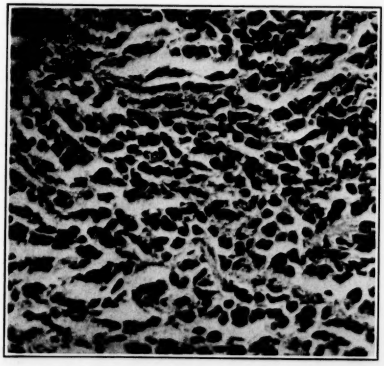

FIGURE 3. *High-Power Magnification.*

The protoplasm of the tumor cells cannot be well recognized. The nuclei seem far away from each other (shrinking). No definite architecture is recognizable.

Except for drowsiness, cyanosis and moderate nausea attributable to the sulfanilamide, the subsequent course was entirely uncomplicated. The abdomen was soft and not distended. The temperature rose to 102.2°F. on the day following operation, and thereafter gradually descended to normal on the 6th day.

The wound healed by primary union. The patient was up and about for several days, and was discharged from the hospital on the 17th postoperative day.

When last examined, 8 months after operation, the patient was quite well. Except for three or four occasions when she experienced moderate abdominal dull pain and discomfort with no associated nausea or vomiting, which were quickly relieved by enema, she had had no symptoms suggesting any disorder related to the disease for which she was operated on. Physical examination was entirely negative; the operative scar was firm, and the abdomen was soft and nontender throughout, with no palpable organs or mass.

Conclusions

Cases of intussusception due to carcinoid tumors are extremely rare.

The case reported appears to be the first record of a carcinoid tumor causing an intussusception of the jejunum.

Carcinoid tumors are more frequently malignant than has been usually assumed, although the rate of progression is slow.

Resection of the involved intestine offers an excellent prognosis for permanent cure, in the absence of distant metastases of the lymph nodes or liver.

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MEDICAL PROGRESS

ENDOSCOPY*

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BOSTON

SINCE there have been several recent articles in the *Journal* on gastroscopy (Benedict,[1] Jankelson and McClure[2]) and peritoneoscopy (Benedict,[3] Garrey[4]), this report is confined to a review of the present status and recent progress in bronchoscopy and esophagoscopy, perhaps better termed "bronchoesophagology" (Jackson[5]).

Bronchoscopy

Bronchoscopic examination was originally developed, and during the early years was performed, for the purpose of removing foreign bodies from the tracheobronchial tree. With increased knowledge of pulmonary disease and greater experience in thoracic surgery, however, bronchoscopy has become of major importance in the diagnosis and treatment of intrapulmonary disease. Approximately only 2 per cent of the bronchoscopies now performed are for the removal of foreign bodies.

Technic

The *sine qua non* of successful bronchoscopy is good teamwork, for with it bronchoscopy is comparatively easy; without it the procedure may be extremely difficult or impossible. When bronchoscopy is made easy, internists and surgeons will request it with almost as little thought as ordering an x-ray examination, and will refer to it as "slipping down a bronchoscope"; when clumsily performed, however, it will seldom be requested a second time, for physicians will not "put their patients through it." Good teamwork means not only a skillful operator but also an experienced head holder and a well-trained nurse in charge of the instruments. Changes in personnel are

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disastrous. Bronchoscopic equipment is delicate and requires constant supervision by experts, for defective apparatus cannot be corrected after the bronchoscope has been introduced. In adults, a preliminary sedation is used with cocainization of the throat; in children, no anesthesia is used. New instruments have been repeatedly designed for special uses by the Jacksons[6] and others, but in general the technic and equipment are well standardized. The use of the telescopic bronchoscope (Pinchin and Morlock,[7] Wolfson and Schloss[8]) has permitted in many cases a clear view into the upper-lobe bronchi. The telescope is passed through the standard bronchoscope, and since its objective lens permits vision at right angles to the axis of the instrument, a view can be obtained into an otherwise inaccessible bronchus. If a lesion is visible, the curved flexible forceps may then be passed to obtain a specimen of tissue.

Anatomy

The nomenclature of the various bronchopulmonary divisions and segments has become of great importance to the bronchoscopist and thoracic surgeon, especially since Churchill's[9] pioneer work on segmental lobectomy. Recent studies have been reported by Neil, Gilmour and Gwynne.[10] Further attempts to standardize the nomenclature are in progress at the Massachusetts General Hospital (Adams and Davenport[11]). Davis[12] has discussed anatomic variations of the normal tracheobronchial tree.

Use in Various Diseases

Bronchiectasis. The diagnosis of bronchiectasis is usually established by the clinical history and x-ray examination after the instillation of iodized oil. Bronchoscopy is indicated when the question of foreign body arises. Hemoptysis, although a frequent symptom in uncomplicated bronchiectasis, may indicate the presence of a benign or malignant tumor partially blocking the bronchus. Although some evidence of tumor is usually present by physical signs or x-ray examination, bronchoscopy is indicated in doubtful cases. At the conclusion of the procedure, a catheter may be placed in the trachea and iodized oil instilled. This method of bronchography has proved more satisfactory than direct instillation through the bronchoscope. Once a diagnosis of bronchiectasis has been established, the treatment, if possible, is lobectomy. When, however, the disease is too extensive or the patient is a poor operative risk, palliative treatment is given by repeated bronchoscopic aspiration. By this method the patient is relieved of large amounts of foul, partially stagnant secretions, is able to breathe better, raises his secretions more easily and gains in weight and strength. When large amounts of foul stagnant secretions are present, bronchoscopy is indicated as a preliminary procedure to lobectomy.

Chronic cystic disease. The indications for bronchoscopy in this disease are much the same as in bronchiectasis. In the inoperable cases, striking improvement is seen after bronchoscopic aspirations repeated about every two weeks.

Asthma. Bronchoscopy in asthma has proved of value in diagnosis and treatment. With regard to diagnosis it should be emphasized that although wheeze is a common symptom in asthma, it occurs in other pulmonary diseases, notably carcinoma, benign tumor and foreign body. Clerf[13] has reported cases with apparent asthmatic wheeze due to carcinoma of the bronchus and foreign body in the esophagus. Whenever any doubt exists, bronchoscopy should be performed. In the treatment of asthma, the procedure has been useful in the aspiration of excessive secretions. Repeated aspiration may be necessary. When atelectasis is present, the bronchoscopic removal of tenacious secretions from the orifice of the involved bronchus may result in re-expansion of the lobe. Bronchostenosis, characterized by febrile episodes, occurred in 68 per cent of the asthma cases recently reported by Prickman and Moersch.[14] In many of these cases, x-ray examination was negative. At bronchoscopy a stenotic bronchus may be visualized and dilated, with aspiration of thick, tenacious secretions. Vaccine made from bronchoscopically removed secretions has been reported to be of value in cases of bacterial allergy.

Chronic bronchitis. Many patients come to the physician because of hemoptysis without other symptoms. In some of these patients, physical examination and complete x-ray study are negative. Bronchoscopy reveals a slightly red, sometimes edematous, friable, easily bleeding mucosa in one or more parts of the tracheobronchial tree. When this mucosa is touched gently with the tip of the bronchoscope, abnormally free oozing of blood occurs. Such a finding accounts for repeated small hemoptyses in these patients. The cauterization of such areas with 5 per cent silver nitrate is apparently of some benefit. Although this disease is not chronic bronchitis in the ordinary sense of the term, it probably represents a mild inflammatory state of the bronchial mucosa.

Acute laryngotracheobronchitis (Richards[15]) is a very serious respiratory disease of children and carries a high mortality. It is characterized by edema, desquamation, and the formation of sticky gelatinous crusts, which cause bronchial obstruction with atelectasis. Tracheotomy may be neces-

sary for laryngeal obstruction, and repeated bronchoscopies are required for the removal of obstructive material.

Diffuse polypoid laryngotracheobronchitis (Samson[16]) is a rare condition characterized by inflammatory polypoid mucosal changes possibly secondary to chronic pulmonary suppuration. Special bronchoscopic curettes have been designed by Samson for rapid removal of the obstructing tissue.

Broncholithiasis, the formation of one or more calcareous deposits in the bronchial tree, is a rare condition and is probably the result of inflammation in the bronchus or erosion of a calcareous peribronchial lymph node. Cough, hemoptysis, wheeze and signs of bronchial obstruction may be present. Bronchoscopy is indicated for accurate diagnosis and removal of the broncholith.

Postoperative pulmonary complications. Postoperative atelectasis frequently clears up spontaneously after severe coughing and changes in the patient's position. When, however, re-expansion does not take place promptly, bronchoscopy is indicated to remove thick tenacious secretions plugging the bronchial orifice. By securing prompt re-expansion of the lobe under such conditions, one may prevent more serious pulmonary complications. Gius[17] has recently reviewed this subject in detail, stating that bronchoscopic aspiration has been repeatedly used with gratifying results. Anesthesiologists (Beecher,[18] Mousel,[19] Eversole[20]) are becoming increasingly aware of the value of tracheobronchial aspiration during and after anesthesia.

Lung abscess. Bronchoscopy is indicated in lung abscess to exclude or remove foreign bodies, to localize exactly the abscess in a particular pulmonary segment, to aspirate secretions and to improve drainage from the abscess cavity. Bronchoscopy sometimes discloses an unsuspected neoplasm in addition to the abscess. Bronchoscopic treatment of lung abscess should be reserved primarily for abscesses that are accessible to the major bronchi. Appropriate medical measures must also be instituted, including rest in bed, adequate diet and postural drainage. If an early response to medical and bronchoscopic treatment is not obtained, surgery is indicated. The management of lung abscess should therefore be in the hands of the internist, roentgenologist, bronchoscopist and thoracic surgeon.

Malignant tumor. The frequency of primary carcinoma of the lung is apparently increasing. A presumptive diagnosis may often be made from the history of cough, hemoptysis and weight loss, together with the physical signs and x-ray findings. A positive diagnosis can be made in about 75 per cent of the cases by bronchoscopic biopsy, and the exact location of the tumor is established. Only by knowing as closely as possible the exact site of the lesion can the proper procedure — lobectomy, pneumonectomy or x-ray therapy — be determined. Removal of large amounts of cancer tissue by bronchoscopy may occasionally be of temporary benefit in improving the airway. The introduction of radon seeds through the bronchoscope is of little value compared to x-ray treatment. If lobectomy or pneumonectomy is not indicated, marked relief of cough, pain and hemorrhage is sometimes obtained by x-ray therapy, particularly in the oat-cell or highly malignant cancers. When life is prolonged over two years by any type of nonsurgical therapy in carcinoma, one must seriously question the diagnosis, for benign adenoma may simulate adenocarcinoma. Metastatic tumors to the lung seldom invade the major bronchi. When they do on rare occasions obstruct a major bronchus, improvement in the airway may be obtained by bronchoscopic removal and x-ray therapy. In the present state of knowledge, the only hope of cure in cancer lies in early diagnosis. For this reason, it is important to perform bronchoscopy early when bronchogenic carcinoma is suspected.

Benign tumor. Adenoma is undoubtedly the commonest benign tumor of the bronchus. Although the history of long-continued hemoptysis in a young patient, in addition to the physical signs and x-ray findings, may lead to a probable diagnosis of adenoma, atypical cases occur frequently enough to make a positive diagnosis possible only by bronchoscopy. When the bronchoscopist sees a smooth rounded tumor mass in the bronchus, he may be reasonably sure that he is dealing with a benign tumor, but sometimes a fairly smooth fingerlike process from a carcinoma may project upward into the bronchus and may be confused with a benign tumor. Bronchoscopic biopsy leads to a positive microscopic diagnosis. If the case is one of benign tumor and irreparable lung damage has not already occurred as a result of bronchial obstruction, bronchoscopic removal of the tumor is indicated. This may require several bronchoscopies, and the site of the tumor should be inspected subsequently at regular intervals to detect possible recurrence. Although a considerable portion of the tumor may lie outside the bronchus, it is nonmalignant, and the patient is entirely relieved by bronchoscopic removal. If irreparable lung damage has occurred and the patient's symptoms and general condition warrant it, lobectomy or pneumonectomy is indicated.

Tuberculosis. Tracheobronchial tuberculosis is encountered with increasing frequency and is therefore of great importance. Its apparent increase is probably due largely to the more frequent use of the bronchoscope. It occurs in approximately 10 per cent of the cases of pulmonary tuberculosis. The old fear that bronchoscopy might cause a spread of the lesion has not been borne out by hundreds of bronchoscopic examinations in various stages of the disease. A persistently positive sputum in the face of essentially negative or minimal x-ray findings may be explained by the bronchoscopic demonstration of ulcerative or proliferative bronchial lesions. Such lesions may heal after the application of silver nitrate, but the fact that they have also been observed to heal spontaneously with probable equal frequency gives little encouragement to the use of intrabronchial applications. Unfortunately these lesions usually do not heal but tend to increase in size, to appear in other locations and to produce bronchial obstruction. In selected cases during the acute congestive stage, x-ray treatment is of benefit (Davenport[21]). Fibrous stenosis from old tracheobronchial tuberculosis may cause symptoms of intermittent bronchial obstruction, namely, cough, fever and malaise, with inability to raise sputum. In such cases, gentle dilatation of the stenosis by soft bougies may relieve the obstruction and cause marked improvement. Bronchiectasis may develop distal to the stenosis. In general, the prognosis of active tracheobronchial tuberculosis is bad. Occasionally tuberculous lymph nodes may by extrinsic pressure on the trachea or bronchi cause partial obstruction. Such lymph nodes may erode the bronchial mucosa, enter the bronchus and cause complete obstruction; they should be removed bronchoscopically.

The following are the indications for bronchoscopy in tuberculosis: obstructive symptoms, that is, atelectasis, wheeze, difficulty in raising sputum, persistent cough or dyspnea out of proportion to the amount of pulmonary disease, periodic intermittent febrile attacks and x-ray evidence of bronchial narrowing; positive sputum when parenchymal disease is controlled or absent; hemorrhage in the absence of sufficient pulmonary disease to explain the source; proposed collapse therapy in those in whom there is any question of tracheal stenosis or stenosis of the contralateral bronchi.

Sarcoid. Pulmonary sarcoidosis is not uncommon. Bronchial involvement by sarcoid was first reported, however, in a recent paper by Benedict and Castleman.[22] In this case, the signs and symptoms of bronchial obstruction were the important features. Bronchoscopy showed extensive intrinsic involvement of the bronchial mucosa. A bronchoscopic biopsy showed the characteristic histology of sarcoid without evidence of tuberculosis. Treatment through the bronchoscope resulted in marked improvement.

Foreign body. Although representing only a small proportion of the work in any bronchoscopic clinic, the removal of foreign bodies is still probably the most dramatic work of the bronchoscopist. Since instruments exist for the removal of all sizes and shapes of vegetal and metallic foreign bodies in children as well as in adults, — not only from the major lower-lobe bronchi but also, with the aid of the biplane fluoroscope and the costophrenic bronchoscope, from the upper lobe and terminal bronchi, — it is evident that few foreign bodies are beyond bronchoscopic removal. Although all foreign bodies should be promptly removed, some metallic foreign bodies have been known to remain in the bronchi for a number of years and, in the absence of bronchial obstruction, to have caused comparatively little lung damage. Since all vegetal substances cause violent mucosal reactions, frequently with complete bronchial or even tracheal obstruction, their removal constitutes a real emergency. A bronchoscopic clinic should, therefore, be in a state of complete preparedness for any emergency.

Esophagoscopy

Technic

The same considerations apply here as were emphasized in the paragraph on bronchoscopic technic. Particularly important is the avoidance of general anesthesia, which is not only unnecessary and more dangerous than local anesthesia but also likely to limit the frequency with which the procedure will be requested.

Use in Various Diseases

Carcinoma. This is by far the most important disease of the esophagus. The first symptom is difficulty in swallowing solid food. Regurgitation of food, saliva and blood is common. Difficulty in swallowing liquids is a late symptom. Pain, if present at all, is usually noted only in the late stages. For an early diagnosis of carcinoma of the esophagus, every patient complaining of dysphagia should have immediate x-ray examination. The x-ray diagnosis of esophageal carcinoma is highly accurate, but confusion has sometimes occurred with benign stricture and with cardiospasm. Esophagoscopy is indicated in every case of suspected cancer of the esophagus. A biopsy can be obtained and the diagnosis thus positively estab-

lished, with grading of the type and degree of malignancy. Moreover, the esophagoscopist may be able to give useful information to the thoracic surgeon regarding possible fixation of the growth. Because of recent advances in the technic of esophagectomy, it is imperative that the diagnosis be established early. I have recently seen two comparatively young patients (forty-two and fifty-seven years of age) in whom the history and x-ray findings were those of carcinoma, but in whom esophagoscopy at another hospital failed to reveal the tumor. These patients were treated for benign stricture until a subsequent esophagoscopy demonstrated carcinoma, when it was too late to operate. Under such circumstances the important thing is to perform repeated esophagoscopies until no doubt remains as to the correct diagnosis.

Many patients, unfortunately, are seen so late in the disease or are such poor surgical risks that operation is not indicated. Much can be done, however, to keep these patients comfortable. The lumen of the esophagus can be kept open by bouginage and x-ray treatment, and since everyone prefers feeding by mouth to being fed by gastrostomy tube, this is very important and saves many needless gastrostomies. Whenever during the course of the disease or as a temporary result of x-ray treatment the lumen of the esophagus becomes so narrowed that only liquids are tolerated, the patient should be instructed to swallow a thread over which bougies may be passed. After about 15 feet of thread has been swallowed, it becomes securely anchored and serves as a guide for the passage of bougies. There is, of course, some danger in stretching an esophagus invaded by cancer, but the risk is worth taking under these circumstances, and in my experience there have been no accidents. I have under my care a young patient with carcinoma of the esophagus (recognized too late for esophagectomy) who could barely swallow liquids on admission but who now can eat normally as a result of bouginage and x-ray treatment. Although he will ultimately succumb to the disease, he is leading a fairly normal life and has returned to work. Such palliative results are definitely worth while.

Benign tumors of the esophagus are exceedingly rare. Patterson,[23] in 1932, was able to find reports of only 61 cases in the literature. Among these are included adenomas, fibromas, lipomas, angiomas, papillomas, leiomyomas and myxomas. The symptoms are usually dysphagia and regurgitation. X-ray examination should show the location of the tumor. Esophagoscopy is necessary for biopsy and removal.

Cardiospasm. This diagnosis is usually made by history and x-ray examination, but in doubtful cases esophagoscopy is occasionally indicated to rule out carcinoma. Although drug therapy and psychotherapy are sometimes of benefit, the most striking improvement usually follows dilatation with mercury bougies. This may have to be repeated at varying intervals. Occasionally in intractable cases the use of the Plummer bag is advisable. Rarely, as in some cases of long-standing cardiospasm with megaesophagus, some type of plastic surgery of the cardia is indicated.

Benign stricture. Stricture of the esophagus may be congenital, the result of lye burn or the result of an inflammatory process. Diagnosis and treatment by esophagoscopy and bouginage are indicated. In any event, carcinoma must be ruled out, since it occasionally develops at the site of congenital or lye stricture (Benedict[24]).

Esophagitis. Some physicians seem surprised when a diagnosis of esophagitis is proposed, but when one looks at the esophageal mucosa through the esophagoscope and finds it red and edematous, sometimes with exudate and mucosal proliferation, there can be no doubt of the existence of an inflammatory process. Such a diagnosis is suggested by substernal pain aggravated by swallowing. Hematemesis is not uncommon. The diagnosis is made only by esophagoscopy. Sometimes the process is so proliferative as to be confused with carcinoma; in such cases, a biopsy will establish the diagnosis, and suitable treatment can be instituted.

Peptic ulcer. Benign ulcers of the esophagus are rare. They occur at the lower end, and cause symptoms similar to gastric or duodenal ulcer. Unless there is a congenitally short esophagus or aberrant gastric mucosa, the term "peptic" is a misnomer. Esophageal ulcer may occur in association with gastric or duodenal ulcers, or with esophagitis, and the process may go on to stenosis (Jackson,[25] Benedict and Daland,[26] Klein and Hochbaum[27]). Esophagoscopy is indicated for diagnosis and treatment.

Foreign body in the esophagus is usually recognized by the history and x-ray examination. Unless the foreign body passes quickly into the stomach, esophagoscopy is indicated to remove it. Because of the danger of perforation, blind bouginage for the purpose of forcing the foreign body into the stomach is to be severely condemned. Pushing the foreign body into the stomach at esophagoscopy is also to be deplored, for it is very rare indeed that a foreign body in the esophagus cannot be safely removed through the mouth. Most foreign bodies that have reached the stomach go through the pylorus and proceed through the intestinal tract

without undue delay. Sometimes, however, large objects fail to pass the pylorus, and certain long and sharp objects may encounter difficulty in following the turns of the intestine. Such foreign bodies may be removed by open-tube gastroscopy or by the use of Tucker's[28] sheathed flexible gastroscopic forceps under biplane fluoroscopic guidance. If perforation of the esophagus occurs either as a result of the character of the foreign body or as a result of instrumentation, radical surgical drainage is indicated to prevent mediastinal abscess.

Varices. Esophageal varices are now commonly recognized by x-ray examination (Schatzki[29]). Since fatal hemorrhage is a frequent occurrence in patients with extensive varices, and since no surgical approach has been successful, injection of sclerosing solutions into the veins through the esophagoscope has been performed by Crafoord and Frenckner[30] and by Walters, Moersch and McKinnon.[31] I have recently treated a patient in this manner.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

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CASE 27141

PRESENTATION OF CASE

First Admission. A fifty-one-year-old woman entered the hospital complaining of abdominal pain.

The patient had a story of generalized abdominal pain localizing in the right lower quadrant, anorexia, constipation and vomiting of two days' duration. The abdomen was tympanitic and quiet, with spasm and marked tenderness in the right lower quadrant; the white-cell count was 11,700, the temperature 100°F. A diagnosis of acute appendicitis was made, and at operation about 100 cc. of thin fecal pus was found in the peritoneal cavity, together with two free-lying fecaliths, the whole contained in a cavity whose lower medial wall was composed of small bowel bound together by thin inflammatory film. The appendix was retrocecal and had a large perforation near its base that had almost transected it. It was resected, and a chromic tie placed about the base; the wound was closed around two cigarette wicks. Postoperatively the patient was given sulfapyridine and two 500-cc. blood transfusions. Purulent material drained from the wound for nine days, and she ran a temperature until the nineteenth postoperative day, generally spiking to 101°F., but occasionally to 102. The white-cell count was 14,000 on the twelfth day, but rapidly became normal. The patient was discharged twenty-four days after admission.

Final Admission (five months later). One month after discharge the patient came to the Out Patient Department for a routine follow-up with the single complaint of gas pains two days previously; physical examination was negative. She was well until six days before admission, when a nonradiating epigastric soreness developed, accompanied by anorexia and nausea. This dull pain soon became generalized and finally localized in the hypogastrium, at which time she suffered from urinary incontinence and burning. The pain continued for two days and was associated with constipation; she took castor oil, which resulted in several bowel movements and great relief. At the time of observation, pain had been absent for two days, although anorexia had persisted. The temperature was found to be 103°F., so that immediate admission was advised.

On examination the patient was well developed and well nourished and in no acute distress. Examination of the heart and lungs was negative; the blood pressure was 115 systolic, 80 diastolic. The abdomen was not tender, and peristalsis was very active. There was slight right costovertebral tenderness. On pelvic and rectal examinations one examiner felt an ill-defined, irregular mass in the right vault.

The temperature was 103°F., the pulse 100, and the respirations 30.

The urine was normal. The blood showed a red-cell count of 4,000,000 with a hemoglobin of 75 per cent, and a white-cell count of 19,900 with 87 per cent polymorphonuclears. The nonprotein nitrogen of the blood serum was 19 mg., the protein 6.7 gm. per 100 cc., the serum van den Bergh slightly above normal (biphasic) and the chlorides 95.5 milliequiv. per liter. Agglutination reactions for typhoid and paratyphoid bacilli and *Brucella abortus* were negative.

A flat abdominal x-ray film showed no dilated loops. There was a moderate amount of gas in the right half of the colon, and a small quantity of gas in the small bowel. A Graham test showed a segment of bowel, apparently the small intestine, unusually high and in front of the liver. A faint shadow of the gall bladder was seen within the shadow of the liver, with a round area of decreased density near the fundus consistent with a cholesterol stone. An x-ray film of the chest showed the diaphragm to be high on both sides, motion being slightly less on the right. The lung fields were clear, and the heart was transverse in position, but not definitely enlarged.

On the third hospital day there were diminished resonance and fremitus at the right lung base, with no rales, but many loud rhonchi and a definite friction rub over the area; the right diaphragm moved fairly well. Slight spasm was present in the right upper quadrant of the abdomen, the liver was 1 cm. below the costal margin and there was right costovertebral tenderness. Five days later the patient was much worse, her eyes were sunken, and she was sweating profusely but complained only of an occasional pleuritic pain in the right posterior chest. The abdomen was tender below the costal margin in the anterior axillary line, and there was some muscle resistance there, but no true spasm. She began to suffer from chills, and the scleras became slightly icteric; pain was referred to the right scapular region. The next day there was tenderness on percussion over the right costal margin; the right diaphragm was

higher than the left and moved hardly at all; coarse rales were present at both lung bases, more pronounced on the right. The white-cell count was 34,000, the hemoglobin 60 per cent.

An operation was performed.

Differential Diagnosis

Dr. Henry H. Faxon: Perhaps we had best start by looking at the x-ray films.

Dr. Aubrey O. Hampton: This plain film of the abdomen shows gas in the right colon.

Dr. Faxon: Is it necessarily in the colon?

Dr. Hampton: Yes. That is the cecum, and this, the hepatic flexure; there is not much gas in the small bowel. However, I do not believe there is enough gas anywhere to be of much significance. It does not indicate obstruction, so far as I can tell. The gall bladder did not concentrate the Graham dye normally, but just enough to show a large nonopaque stone.

Dr. Faxon: In the record it says, "A Graham test showed a segment of bowel, apparently the small intestine, unusually high and in front of the liver."

Dr. Hampton: I do not get that impression. These bubbles could be in the colon. I do not consider the condition abnormal.

Dr. Faxon: And the shadow that you see there is almost certainly a gallstone?

Dr. Hampton: Yes. It maintains its relation with a faint shadow of the gall bladder. I think we can be fairly certain that there is a stone.

Dr. Faxon: When I first read the report, I considered the possibility whether the shadow described in the region of the liver could be an abscess cavity in the liver rather than a gall bladder with stone.

Dr. Hampton: I do not believe that it could.

Dr. Faxon: We have a fifty-one-year-old woman with the classic signs of acute infection, which we can readily localize within certain limits. In cases in which a liver abscess or a subphrenic abscess is suspected, the differential diagnosis is often further confused by the presence of chest signs or symptoms that make it difficult to decide whether the process is above or below the diaphragm. In this case, from the past history, from the earlier x-ray studies and from the chest examination, we can safely conclude that the infectious process is not in the chest itself. The diaphragm was limited and high, and the patient had some pleuritic pain, but these findings could certainly be accounted for by irritation below the diaphragm.

Is there anything to suggest that the infectious process might be in the kidney? We have the finding of costovertebral tenderness on one occasion, and also a note of burning and frequency of urination. I think it is worth pointing out that one should not jump to the conclusion that costovertebral tenderness is of necessity due to disease of the kidney. With a subphrenic abscess one of the most typical findings is tenderness in that region, more especially brought out by pressure over the twelfth rib than by pressure in the angle itself. Inasmuch as later in the story the urine was negative and the nonprotein nitrogen normal, it seems to me that we can rule out the kidney as the site of this infection.

What part might the intestinal tract have played in the symptomatology? The crampy pain, the hyperactive peristalsis on examination and the relief from discomfort with bowel movements all suggest the possibility of obstruction. However, obstruction would not account for the high temperature and persistently high white-cell count. I think it is more than possible that in the walling off of the original inflammatory process the patient may have developed adhesions between loops of small intestine that gave rise to a certain degree of subacute obstruction accounting for the early symptoms one month after her discharge from the hospital; these adhesions may have been a contributing but relatively unimportant factor when she came in at this admission.

That brings us to the gall bladder. We have the story of right-upper-quadrant pain, with radiation to the right posterior chest. We have jaundice as the disease progressed, and furthermore we have the perfectly definite finding by Graham test of a stone in the gall bladder. Can the whole picture be accounted for on the basis of cholecystitis and cholelithiasis? It seems to me that with such a high white-cell count and temperature, there would have been more striking physical signs in the gall-bladder region if the pathologic process had been confined to that area. One of the early signs was tenderness in the costovertebral region rather than in the anterior part of the abdomen, and as the story progresses the tenderness and spasm were almost always well lateral and posterior rather than in the region of the gall bladder itself. I do not believe, therefore, although the patient had a definite stone, that cholecystitis and cholelithiasis were the main factors in this case.

With the antecedent story of ruptured appendix, we come down to a differential diagnosis between subphrenic abscess and liver abscess secondary to pylephlebitis. It may seem to be of somewhat academic interest to try to make a distinction between these two conditions, but as a matter of fact it is of extreme practical importance to the surgeon if he is going to drain the area to know which of the two situations exists. In favor of

liver abscess we have as the most significant thing about the first entry with its operation for her ruptured appendix the fact that the temperature, instead of returning to normal, persisted around 101 and 102°F. for a period of over two weeks. Before operation on the second admission, the patient had chills and jaundice; the diaphragm, which was elevated but not fixed at first, later became almost fixed, and the liver was said to be enlarged. It might be of interest to pause a moment and consider the incidence of chills in relation to pylephlebitis in association with appendicitis. Of the cases of ruptured appendices in this hospital, approximately 10 per cent gave a history of chills prior to operation. Only 10 per cent of these, however, went on to develop pylephlebitis. On the other hand, of the patients who are known to have had pylephlebitis, almost all at some time in the course of the disease complained of chills. The incidence of pylephlebitis and liver abscess with acute appendicitis is approximately 0.5 per cent. So much for the possibility of liver abscess.

What evidence have we to endorse a subphrenic abscess as the cause of this patient's symptoms? Again we have the history of ruptured appendix, on the first admission, with thin pus and two fecaliths free in the peritoneal cavity. The thin pus could have been aspirated into the subdiaphragmatic region, since the pressure in the upper abdomen with quiet respirations is less than that in the lower portion. If there were two fecaliths, there might have been a third that could have served as a focus for persistent infection and possible abscess formation. The incidence of subphrenic abscess with acute appendicitis is about twice that of pylephlebitis. The high diaphragm, which is a finding that is almost always present with a subphrenic abscess, is present in about half the cases of liver abscess. However, the motion of the diaphragm is far more apt to be restricted or absent with a subphrenic abscess than with a liver abscess. The objection might be raised in considering these two diagnoses that, because of the long interval between the inciting appendectomy with drainage and the subsequent development of the condition that the patient showed, they could be excluded. It was of interest to me in reviewing the cases of subphrenic abscess in this hospital since 1900, however, to find that almost 10 per cent of the patients gave a story of over three months from the time of the inciting cause to the time of the drainage of the abscess. It is only fair to say that many of the long delayed cases were in the early years of that period and far fewer in the later years.

From the history as given here, I should think that we must explain in some way the change in the picture from apparent health to illness that occurred six days prior to entry. Had it been a subphrenic abscess from the start, I do not believe there would have been so abrupt and sudden an onset six days before the patient came in the second time. The only way that I can rationalize that short story on the basis of either a liver or subphrenic abscess is to assume that the collection of pus that had developed secondary to the first operation ruptured or leaked six days prior to the time that she came in. The fact that there were so few signs in the chest at the time of entry is against a long-standing subphrenic abscess. This is not inconsistent with long-standing liver abscess, and I believe that what happened in this case was that the patient had a gangrenous appendix, developing a subclinical pylephlebitis with a residual liver abscess, and that the abscess had smoldered along for five months and finally came to the surface of the liver, either to leak or to cause further irritation in one of the subphrenic spaces.

My diagnosis is liver abscess, with secondary subphrenic abscess and the incidental findings of cholelithiasis and pleuritis.

Dr. Oliver Cope: This patient's second admission came when I was on service. The history is a bit misleading, although it is the history that she gave. She was a very uncomplaining woman, and it was only on further questioning after the preliminary studies had been made that we found out what had happened before the onset of the immediate symptoms bringing her to the hospital. It was obvious that she had never been well from the time of the first admission and that her difficulties were due to a complication after appendicitis, even though it was five months from the time of the ruptured appendix. We argued, like Dr. Faxon, that it must be either liver abscess or subphrenic abscess. There were not sufficient signs immediately, but when the temperature began spiking and the van den Bergh became positive (the jaundice was not really noticeable clinically), we suspected that it was a liver abscess. Dr. Howard Ulfelder operated on the patient, and I scrubbed up with him. He made a diagnosis of liver abscess. I was not sure it was not subphrenic abscess in view of the positive signs that she showed. It turned out that it was quite a large liver abscess. Dr. Ulfelder resected the twelfth rib on the right side and then inserted a needle in two or three places. Finally pus was found. There was nearly a centimeter of uninvolved liver protecting the subphrenic space, but in spite of that there was considerable edema and inflamma-

tion on the undersurface of the diaphragm, so that there was really an incipient subdiaphragmatic abscess. This inflammation accounted for the chest signs. We suspected that there might be other abscesses, even though the abscess cavity was at least 10 cm. in diameter.

The postoperative course was stormy. The infection was progressively severe and overwhelming; the patient died in spite of chemotherapy nine days after drainage of the abscess. The chart is interesting. During the week she was in the hospital before operation the temperature climbed to 103°F. After the operation the temperature dropped to normal for several days, but clinically the patient did not improve so much as the drop in temperature indicated. The pulse was 100 to 120, and there was a terminal abrupt rise. We suspected that we had drained only one of several abscesses within the liver.

Clinical Diagnoses

Liver abscess.
Subdiaphragmatic abscess.

Dr. Faxon's Diagnoses

Liver abscess, with secondary subdiaphragmatic abscess.
Cholelithiasis.
Pleuritis.

Anatomical Diagnoses

Multiple abscesses of the liver.
Peritonitis, acute fibrinopurulent.
Icterus.
Cholelithiasis.
Leiomyoma of uterus.
Surgical wounds: appendectomy; drainage of liver abscess.

Pathological Discussion

Dr. Tracy B. Mallory: The autopsy showed numerous other abscesses. There were two large ones and a very considerable number of abscesses 0.5 to 1 cm. in size. It would obviously have been impossible to drain the major proportion of them. The autopsy was limited to the abdomen, so that I cannot say whether there was a pleuritis or not. The portal vein was dissected with care, and no evidence of thrombosis could be made out. A rather unexpected finding at autopsy was a severe general peritonitis. This was evidently of some duration, since most of the pus was in well-isolated pockets and there was very little fluid free in the peritoneal cavity. Some of the localized pockets were of considerable size, including one 6 cm. in diameter just lateral to the cecum. At what time peritonitis developed I do not believe we can say — presumably very close to the time the abscess was drained but whether before or after I do not know.

Dr. Cope: The general peritonitis was a surprise to us. We did not clinically appreciate it. Whether it had any relation to the obstipation and the catharsis that the patient had had before coming in we do not know. Another possible source of the peritonitis is that, since we obviously opened into a clear fascial plane above and behind the liver, we opened new pathways to infection that had not existed at the time of the ruptured appendix. Do Dr. Mallory and Dr. Faxon agree that we were right in assuming that the liver abscesses were the result of portal-vein infection?

Dr. Mallory: I think there is very little doubt that that must have been the pathway of infection. It was presumably a matter of metastasis of a few organisms rather than an ascending thrombophlebitis.

To conclude: a gallstone was present. We found no organic obstruction of the bowel. The only other finding was a moderately large fibroid of the uterus, which was evidently the mass that one examiner found on pelvic examination.

Dr. Faxon: May I ask Dr. Hampton if there is any way of showing a cavity of that size in the liver by x-ray?

Dr. Hampton: Yes, when it is filled with gas or when Thorotrast is given.

CASE 27142

Presentation of Case

First Admission. A fifty-five-year-old Swedish-American shovel polisher entered the hospital for study.

While working one hot day nine months before admission, the patient felt drowsy and stated that he was unable to sweat; several of his colleagues were similarly affected. Since that time he had been troubled with a nocturia of twice a night, and for the next two months his skin was dry and never perspired. Two months before entry, a pleuritic pain developed over the third and fourth ribs in the right anterior axillary line, accompanied by a slight cough with a small amount of white sputum. The following day his physician recorded an elevated temperature and a pulse of 100, with a few rales at the right apex. Strapping the chest eased the pain, which disappeared in three or four days. A few days later, the patient caught cold, and again there was cough with slight sputum, but no pain; these symptoms continued for a month, and he was weak and slightly dyspneic on exertion and was forced to give up working. Three weeks before admission his physician noted occasional rales and wheezing in both lungs.

The sputum was said to have been negative for tubercle bacilli, and an x-ray film of the chest showed clear apices and no pleural fluid, but a soft density and small calcified nodules in both lung roots. There was no gross consolidation or cavitation. Four days prior to entry a "sore spot" developed below the left costal margin, and pressure over this point gave pain in the right shoulder. In a period of half an hour the soreness gradually shifted across the epigastrium to below the right costal margin and from there to the ribs above the costovertebral angle. It was aggravated by deep breathing, when pain was also noticed in the right shoulder. Strapping the chest again gave relief. His physician stated that the patient's skin had grown darker during the previous six months. He had lost 15 pounds in weight.

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The patient had had gonorrhea at twenty-eight, and fifteen years before entry "rheumatism" for ten weeks, characterized by pain without swelling, first in the knees, then "all over the body."

On examination the patient was a rather poorly nourished red-haired man with freckled pigmentation of the skin, but not of the mucous membranes. The eyes were prominent, with widened palpebral fissures and lid-lag; the thyroid gland was not enlarged. The nasopharynx was reddened. The chest was somewhat barrel-shaped, and tenderness was present over the lateral edge of the right trapezius muscle in the neck. Percussion posteriorly revealed a 4-cm. excursion of the diaphragm on the left, with none on the right. Posteriorly dullness was present to the ninth rib on the left, and to the seventh rib rising into the axilla on the right; anteriorly the upper border of dullness reached the fourth rib on the right. On auscultation the left lung was clear, but on the right there were diminished breath sounds and vocal resonance over the area of dullness, with a few coarse rales immediately above it. The heart was normal; the blood pressure was 135 systolic, 95 diastolic. The liver was palpable four finger-breadths below the costal margin in the midclavicular line. There was a slight tremor of the hands. Rectal examination was negative.

The temperature was 97°F., the pulse 90, and the respirations 20.

The urine showed a ++++ sugar reaction. Examination of the blood showed a red-cell count of 5,200,000 with a hemoglobin of 99 per cent, and a white-cell count of 8500 with a normal differential. The fasting blood sugar ranged from 138 to 185 mg. per 100 cc. A bromsulfalein test was normal, and a formol-gel test showed minimal gelling in twenty-four hours. The blood Hinton reaction was negative. Examination of the sputum and stools was negative. Determinations of the basal metabolic rate gave readings of +39 and +33 per cent. A biopsy of the skin was normal.

An x-ray film of the chest showed the right diaphragm to be elevated, with only a very small respiratory excursion. There were several plate-like foci of atelectasis, and one of these areas arose from a triangular shadow that lay close to the pleural surface. There was no definite evidence of fluid, and the lung fields were otherwise not remarkable. The size of the heart was at the upper limits of normal, and there was calcification of the aorta. A week later the right diaphragm was normal in position, with normal respiratory motion. No fluid was visible, and the lung field appeared normal.

A flat film of the upper abdomen showed the lower border of the liver to be slightly lower than usual, particularly on the left side. The spleen was not enlarged. There were several areas of calcification in the region of the lower edge of the liver on the right side, as well as an area of calcification behind the stomach on the left. Gallstones were thought to be the most probable explanation for the calcified areas on the right side. There was no evidence of varices in the esophagus.

The patient was iodized, and the diabetes brought under control with insulin. A subtotal thyroidectomy for hyperthyroidism was performed three weeks after admission. He was discharged one week later on a diabetic diet with no insulin.

Second Admission (eight months later). The patient was seen three weeks after discharge and had improved very satisfactorily. His appetite was good, and he had gained in weight and strength. There was no tremor, nervousness, palpitation, excessive thirst or frequency, though a nocturia of once a night was still present. A moderate edema about both eyes was noted, and the right eye was still a bit prominent, without lid-lag. The heart was slow and regular, the blood pressure 140 systolic, 108 diastolic, and the basal metabolism rate −2 per cent. Two months later, the findings were the same, but the urine gave an orange sugar reaction, and the blood sugar was 210 mg. per 100 cc., so that insulin therapy was instituted. Four months before admission, the patient began to suffer from fatigue; his legs felt tired and heavy, with a "numb feeling" at the instep of the right foot. In addition, he noticed transient spells of "wooziness," with a staggering gait lasting but a few seconds. Six weeks before entry, he noticed that his skin was becoming dry and scaly. At the time of admission, he volunteered in a slow, deep, husky voice that he worked and thought more slowly than before, and complained of constipation and a dislike of cold weather. It ap-

peared that from the time of discharge until one month before admission the patient had suffered from cramps in his calves and forearms when they were exercised. He had gained 32 pounds since operation.

On examination the skin was dry, rough and scaly, and had a slight yellowish tinge. The heart and lungs were normal, the blood pressure 140 systolic, 90 diastolic. The liver was palpable three fingerbreadths below the costal margin.

The temperature was 97.8°F., the pulse 67, and the respirations 18.

The fasting blood sugar varied from 112 to 296 mg. per 100 cc.; the nonprotein nitrogen of the blood serum was 21 mg. per 100 cc., the carbon dioxide combining power 33 milliequiv. per liter, and the total cholesterol 150 mg. per 100 cc. Bromsulfalein and formol-gel tests were negative. A glucose-insulin tolerance test showed slight resistance to insulin.

The basal metabolism rate varied from −14 to −30 per cent. X-ray examination of the chest showed the heart size to be within the upper limits of normal. The aorta was calcified, but not dilated, and the lung fields showed slight increase in the lung markings.

The patient was discharged two weeks after admission on thyroid, a diabetic diet and 20 units of protamine insulin daily.

Final Admission (one year later). The patient was followed in the Out Patient Department and remained well, although the dosage of thyroid had to be increased to combat the symptoms of myxedema. Suddenly four days before admission general malaise, headache, muscle pains and backache developed, with a slight cough and a temperature of 102°F. Two days later he became weak, drowsy and difficult to manage; he refused to eat, and his cough increased. At the time of admission it was found that he had not taken insulin for at least a month.

On examination the patient was drowsy, uncooperative and coughed frequently. There was facial telangiectasia, with cyanosis and a curious slate-colored pigmentation of the dry skin. The nasopharynx was reddened and edematous. Many rales were heard throughout the chest, being most marked over the right lower lobe, but there was no evidence of consolidation. The heart was normal, the blood pressure 100 systolic, 64 diastolic. The liver was palpable 4 cm. below the costal margin. The reflexes were slow and deliberate, but equal.

The temperature was normal, the pulse 95, and the respirations 20.

The urine showed a ++++ test for albumin, an olive sugar reaction and a ++ test for acetone. Examination of the blood showed a red-cell count of 3,750,000 with a hemoglobin of 11 gm. (photoelectric-cell technic), and a white-cell count of 13,100 with 82 per cent polymorphonuclears. The blood sugar was 392 mg. per 100 cc., and the carbon dioxide combining power 21.9 milliequiv. and the total base 154.5 milliequiv. per liter; the pH was 7.36. The nonprotein nitrogen of the blood serum was 35 mg. per 100 cc.

The day after admission, definite signs of consolidation had developed in the right lower lobe, with scattered areas in the left lung. The temperature had risen to 103°F., the pulse to 130 and the respirations to 30. Chemotherapy was instituted, but the patient failed rapidly and died on the fourth hospital day.

Differential Diagnosis

Dr. John R. Graham: This man was a shovel polisher. It is a trade of which I have never heard, and whether it offers an occupational hazard I do not know. So far as I can make out, the past history is inconsequent. At the first admission it was evident that the patient had a protean collection of symptoms involving several systems of the body. The increased frequency of urination fits with the presence of sugar in the urine, and the high blood-sugar level serves to establish a diagnosis of diabetes. Secondly, the eye signs, the rapid pulse rate and the elevated metabolic rate point to a diagnosis of hyperthyroidism. I am sorry that the record does not include a figure for the basal metabolic rate after iodine had been administered, which would have been conclusive evidence of this diagnosis, but since a thyroidectomy was performed I think we may assume that the response to iodine was what might have been expected. From the physical examination we learn that the liver edge was palpable four fingerbreadths below the costal margin, and with such a finding I believe we are safe in assuming that the liver was enlarged. In this connection it is interesting to note that a biopsy of the skin was performed, and despite the statement of the patient's physician that his skin had become darker no abnormal pigment was observed. Finally we have a puzzling group of signs and symptoms in the chest. One wonders if the dyspnea was due to the pulmonary process or to the hyperthyroidism. I should assume that the calcified nodules near the lung root meant old tuberculosis. The sign at the right base might have been due to a high fixed diaphragm, with atelectasis or a small collection of fluid, or to a consolidating process of the right lower lobe. The evidence of the chart and the normal white-cell count

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are against any very acute infection. The patient had had two or three episodes, each associated with pleural pain, increased dyspnea and sufficient disability to lead him to stop working. It seems to me that a series of pulmonary infarcts was the most likely explanation of what was going on in the chest, and the description of the x-ray findings was found consistent with this diagnosis. After operation it is evident that the symptoms of hyperthyroidism definitely regressed. Moreover it is interesting that despite the removal of the thyroid gland the diabetes apparently progressed, since insulin became necessary. The numbness complained of in the right foot may have been evidence of diabetic neuritis. At the second entry, it is evident that myxedema had developed, and it seems probable that this was secondary to the preceding thyroidectomy. The liver situation had apparently not changed significantly.

Four days before his final admission, the patient had symptoms that sound like an acute respiratory infection rather than infarct, which could hardly explain the headache, muscle pains and backache. I have little doubt that it was pneumonia. The diabetes was certainly no better. It is hard to say whether it had progressed or not. The patient seems to have been in mild acidosis. We have the added information of slate-colored pigmentation to the skin.

In trying to put this whole picture together, I find that it is hard to make all the symptoms and signs conform to one picture. There seems to be a fundamental triad of symptoms that cannot be neglected, namely, diabetes, enlargement of the liver and slate-colored pigmentation of the skin. Hemochromatosis seems to be the only thing to explain these symptoms in one patient. I have never heard of hyperthyroidism with hemochromatosis, and I can only regard this as a coincidence. We know that, in hemochromatosis, primary carcinoma of the liver is a complication in not a few cases, but I see no particular reason why we should make this diagnosis in the present case. My primary diagnosis is hemochromatosis, with pigmentation of the skin and viscera, cirrhosis of the liver and cirrhosis of the pancreas; additional diagnoses are myxedema secondary to operation, gallstones, deep phlebitis in the legs, an old process in the lungs, perhaps due to infarcts, probably some arteriosclerosis on a diabetic basis, a terminal pneumonia and diabetic acidosis.

Dr. Eugene Sullivan: There are one or two points worth mentioning about the case. I sent this patient in at the second admission. At that time he had spent four hours in the Out Patient Department, which is well heated ordinarily, yet he still had his overcoat on. It took about five minutes to get a deep husky answer to any question. It is of some interest that he had been followed sporadically in the medical clinic during the preceding eight months without the detection of definite signs of myxedema. When he arrived on the wards the basal metabolic rate was recorded as low as −30 per cent. He had a well-developed myxedema. He was admitted with the added diagnosis of hemochromatosis, largely because I had the advantage of seeing a pathological report neatly tucked into the record of the first admission. Apparently not much attention had been paid to it, but there existed a careful description of hemochromatosis involving the thyroid gland. At the time I pondered whether the myxedema was partly on the basis of surgical ablation, and partly due to involvement of the remaining epithelial cells of the thyroid gland with the pigment deposit. However, most people believe that hemochromatosis affects functionally only the pancreas and the liver. After the patient arrived for his last admission I saw him in the Emergency Ward. He was sent in as a probable case of diabetic coma. It was obvious that it was not diabetic coma. He was cyanotic and mildly acidotic. He had only an olive sugar test in the urine and was a very ill man. He was so ill that although we thought he had a pneumonic infection, we were hesitant to give chemotherapy because we thought he could not stand anything at the moment except oxygen and warmth. We gave him small amounts of insulin —20 units all told. We discovered that he had taken no insulin during the previous four weeks. We marveled how he had been able to get through a whole month without insulin, and moreover to contract pneumonia, without going into diabetic coma. Several possible explanations were considered. First, a myxedema due to insufficient thyroid medication might have affected the diabetes. Secondly, regarding cirrhosis of the liver, we know that people with diabetes who develop cirrhosis may get over their diabetes clinically. Thirdly, we considered the possible effects of hemochromatosis involving the pituitary gland. Here was pigment deposit in the pancreas producing the picture of diabetes. Would hemochromatosis later involving the epithelial cells of the pituitary gland remove its diabetogenic function? There was no way of settling these points, but they made nice subjects for discussion.

Clinical Diagnoses

Hemochromatosis.
Pneumonia.
Diabetes.
Myxedema.

Dr. Graham's Diagnoses

Hemochromatosis, with skin pigmentation and cirrhosis of liver and pancreas.
Myxedema, postoperative.
Diabetes, with acidosis.
Gallstones.
Pulmonary infarcts, old.
Deep phlebitis of legs.
Arteriosclerosis?
Pneumonia, terminal.

Anatomical Diagnoses

Hemochromatosis, involving liver, pancreas, thyroid gland and lymph nodes.
Myxedema, postoperative.
Bronchopneumonia, confluent.
Pleuritis, healed fibrous.
Icterus, slight.
Telangiectasia of face.

Pathological Discussion

Dr. Tracy B. Mallory: I must confess to having withheld some information from Dr. Graham. At the time of thyroidectomy we did find very large amounts of hemosiderin in the stroma of the thyroid gland—so much, in fact, that we made a diagnosis of hemochromatosis. Otherwise the histologic appearance of the thyroid gland was consistent with a true hyperthyroidism and iodine involution.

At the time of autopsy we found a considerably enlarged, very finely granular and quite tough liver, which was of an abnormal red-brown color. The lymph nodes at the hilus of the liver were deep brown, the pancreas very distinctly brown; so that it was quite easy to make a gross diagnosis of hemochromatosis. Sections of all these organs dropped in a solution of potassium ferrocyanide and hydrochloric acid turned intense blue. Sections of the various endocrine glands were put through to see how extensive the iron deposits might be. The condition in the remaining part of the thyroid gland was essentially the same as at the time of operation. There was a small amount of pigment in the adrenal glands, virtually none in the pituitary gland. The pancreas showed a lot of pigmentation, but much more in the parenchymal cells than in the islet cells. We had again no luck in demonstrating iron in the skin, probably because of poor selection of the specimen for examination.

The mechanism of death was an extensive bronchopneumonia, and I am afraid we were so impressed with the pneumonia that we forgot to look for the scars of the infarcts, which the patient very well may have had. An ordinary routine examination of the lungs post mortem would certainly not rule out healed infarct.

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The Journal does not hold itself responsible for statements made by any contributor.

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ADULTERATED SULFATHIAZOLE TABLETS

For some unexplained reason two or more lots of 0.5-gm. (7.7-gr.) sulfathiazole tablets released by the Winthrop Chemical Company, New York City, in December, 1940, contain a certain number of tablets that are composed, either in whole or in part, of phenobarbital. Practically all the bottles in these lots have been reclaimed from distributing houses, retail druggists and hospitals by representatives of the Winthrop Chemical Company and by inspectors of the United States Food and Drug Administration, but it seems likely that some are still in the hands of druggists, physicians and patients. The impure or suspicious lots are designated "MP," stamped in red ink on the upper right-hand corner of the label on the bottle; the two known to be adulterated are labeled "MP 029" and "MP 118" respectively.

Although the administration of the adulterated tablets produces severe narcosis, practically all such patients have eventually recovered, and the chief danger lies in their use in cases of pneumonia or of other infectious diseases in which the patients are already gravely ill.

Several nonfatal cases have been reported in the vicinity of Boston, and any physician in New England, with the exception of those in the western half of Connecticut, who notes an unexplained and rapid loss of consciousness in a patient following the ingestion of a 0.5-gm. (7.7-gr.) tablet of sulfathiazole should immediately report the fact to Inspector C. C. Sullivan of the United States Food and Drug Administration, Federal Security Agency, 408 Atlantic Avenue, Boston (HANcock 8890).

JOHN GILLIES PRIESTLEY

The *British Medical Journal* for February 22 brings the unhappy news of the death of John Gillies Priestley on February 9. Educated at Eton and later at Christ Church, Oxford, Priestley, at the turn of the century, came under the influence of John Scott Haldane, whose friendship and early guidance determined his future career. He joined Haldane in a series of memorable investigations, the first fruit of which, issued in the *Journal of Physiology* in 1905 under the title, "The Regulation of the Lung-Ventilation," has become one of the classics of modern physiology, for it established the importance of carbon dioxide pressure in regulating the activity of the respiratory center. After this paper was published, Priestley proceeded to St. Bartholomew's Hospital in London to complete his medical qualifications, but shortly thereafter he fell ill and was obliged to spend several years in Switzerland.

Priestley was a keen sportsman and a man of unusual critical capacity. He had deep loyalties, and it was characteristic of him that, despite frail health, he volunteered immediately when World War I broke out, being commissioned on Septem-

ber 1, 1914, after which he served in France and Belgium. In 1915 he received the Military Cross and was also mentioned in official dispatches. Later in the same year he was called to England, where his training in the physiology of respiration was put to use in an important research on the aftereffects of war-gas poisoning. At the end of the war, he settled down at Oxford, and many students will recall his friendly interest and the warm hospitality of the Manor House, where he lived at March Baldon, near Oxford. They will also remember his unyielding insistence on the importance of objective evidence. He was joint author with Haldane of a laboratory text entitled *Human Physiology: A practical course*, and he joined Haldane in the preparation of the second edition of *Respiration*, a book based on the Silliman Lectures given at Yale University by Dr. Haldane.

Priestley rendered invaluable service to the Physiological Society in the preparation of a subject index of the first sixty volumes of the journal, and he succeeded his chief, Professor John Mellanby, as editor of *Physiological Abstracts*. He was responsible for the introduction of the international system of decimal classification of the scientific papers for the *Abstracts* and also for the papers in the *Journal of Physiology*. In the latter attempt to systematize the literature of physiology he had the enthusiastic support and co-operation of Sir Charles Sherrington. Priestley had broad interests in problems of general metabolism and of muscular exercise and in methods for determining cardiac output, a paper on the last subject having been published some two months prior to his death.

MEDICAL EPONYM

Heberden's Nodes

The following is not a partial translated quotation, but represents the entire commentary made by William Heberden (1710–1801) on the nodes that perpetuate his name. It appears in his *Commentarii de Morborum Historia et Curatione* [*Commentaries on the History and Cure of Disease*] (Fourth edition, London, 1816).

> What are those little hard knobs, about the size of a small pea, which are frequently seen on the fingers, particularly a little below the top, near the joint? They have no connection with the gout, being found in persons who never had it; they continue for life; and being hardly ever attended with pain, or disposed to become sores, are rather unsightly, than inconvenient, though they must be some little hindrance to the free use of the fingers.
>
> R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

Raymond S. Titus, M.D., *Secretary*
330 Dartmouth Street
Boston

A Fatal Abdominal Complication in Pregnancy

A twenty-nine-year-old housewife consulted her family physician at the end of the third month of her third pregnancy.

She had had no children, the first two pregnancies having resulted, respectively, in a premature labor at six months and an abortion at two months. She had been operated on five years previously for chronic appendicitis. The past history was otherwise noncontributory.

Physical examination at the time of her first visit was negative. The heart was not enlarged; there were no murmurs. The lungs were clear and resonant; there were no rales. The blood pressure was 120 systolic, 60 diastolic. Vaginal examination showed the uterus anterior and enlarged to a size consistent with the period of amenorrhea.

When the patient was about six months pregnant, she became severely ill, with nausea, vomiting and abdominal pain, the pregnancy previously having been normal. She was seen daily by her physician because of the nausea and vomiting, and since enemas gave no relief, she was eventually sent to the hospital, where she was seen by a surgeon in consultation. At his first visit he believed that there was no surgical condition, and ascribed the nausea and vomiting to toxemia of pregnancy. Two days later, however, fecal vomiting occurred, and there was very definite tenderness in the right hypogastrium. A laparotomy was immediately performed and revealed a twisted loop of large intestine, which was necrotic. This piece of intestine came away on manipulation, and both ends of the large bowel were brought out through an

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

opening in the abdominal wall. The patient died ten days after the onset of symptoms and forty-eight hours after operation.

Comment. This case represents the importance of appreciating the significance of nausea, vomiting and abdominal pain during pregnancy. Had this woman not been pregnant, there is little doubt that the surgeon would have considered an exploratory laparotomy necessary because of a provisional diagnosis of intestinal obstruction. There is no evidence in the record of a temperature reading or a white-cell count when the surgeon first saw the patient. It is possible that there was no fever, but it is quite unlikely that there was no leukocytosis. Too frequently all symptoms during pregnancy are ill-advisedly assumed to be due to pregnancy. A surgical abdomen is a surgical abdomen, whether it occurs in a man or a pregnant woman, and the sooner such abdomens are opened, even if an occasional one is opened unnecessarily, the sooner the number of deaths occurring from surgical complications will be reduced.

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MEDICAL POSTGRADUATE EXTENSION COURSES

The following sessions, given by the Massachusetts Medical Society in co-operation with the Massachusetts Department of Public Health, the United States Public Health Service and the Federal Children's Bureau, have been arranged for the week beginning April 6:

BERKSHIRE

Thursday, April 10, at 4:30 p.m., in the Bishop Memorial Building, Pittsfield. Pediatric Case Discussions. Instructor: Clement A. Smith. Harry G. Mellen, *Chairman.*

BRISTOL SOUTH (Fall River Section)

Tuesday, April 8, at 4:30 p.m., at the Union Hospital, Fall River. The Clinical Recognition of the Types of Jaundice and Recent Advances in Their Treatment. Instructor: Franz Ingelfinger. Howard P. Sawyer, *Chairman.*

FRANKLIN

Thursday, April 10, at 8:00 p.m., in the Library of the Franklin County Public Hospital, Greenfield. Obstetric Complications with Case Histories and Clinical Problems. Instructor: John Rock. Halbert G. Stetson, *Chairman.*

HAMPDEN

Wednesday, April 9, at 4:00 p.m., at the Academy of Medicine, Professional Building, 20 Maple Street, Springfield, and 8:00 p.m., in the Outpatient Department of the Skinner Clinic, Holyoke Hospital, Holyoke. Head Colds and Complications. Instructor: John R. Richardson. Alfonso A. Palermo, *Chairman.*

HAMPSHIRE

Thursday, April 10, at 4:15 p.m., in the Nurses' Home of the Cooley Dickinson Hospital, Northampton. Chemotherapy in the Treatment of Gonococcal Infection. Instructor: P. N. Papas. Robert C. Byrne, *Chairman.*

WORCESTER

Tuesday, April 8, at 8:30 p.m., in the Nurses' Home of the Milford Hospital, Milford. Obstetric Complications with Case Histories and Clinical Problems. Instructor: Roy J. Heffernan. Joseph Ashkins, *Chairman.*

WORCESTER NORTH

Friday, April 11, at 4:30 p.m., in the Nurses' Home of the Burbank Hospital, Fitchburg. Infections of the Hands and Feet. Instructor: Henry C. Marble. George P. Keaveny, *Chairman.*

DEATHS

BOOTH — ERNEST L. BOOTH, M.D., of East Boston, died March 24. He was in his fifty-eighth year.

Dr. Booth attended Boston Latin School and Harvard University and received his degree from Harvard Medical School in 1908. For more than thirty years he was a school physician in Boston, and had been physician for the East Boston plant of the General Electric Company and medical examiner for three insurance companies. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow, two sons and two daughters survive him.

HOYT — EDWARD M. HOYT, M.D., of Georgetown, died March 28. He was in his eighty-fourth year.

Born in Wentworth, New Hampshire, he received his degree from Harvard Medical School in 1894. He spent a few months studying at the Rotunda Hospital in Dublin, Ireland, before starting practice in Georgetown.

Dr. Hoyt was a member of the Massachusetts Medical Society and the American Medical Association, having retired from active practice in 1936.

CORRESPONDENCE

REGIONAL FRACTURE COMMITTEES OF THE AMERICAN COLLEGE OF SURGEONS IN NEW ENGLAND

To the Editor: It might be of interest to readers of the *Journal* to know that the regional fracture committees of the American College of Surgeons in New England are endeavoring to improve the treatment of fractures.

Among the ninety-two of these regional fracture committees now operating in the United States and Canada, New England can boast of six: one for each state. Formed originally to call to the attention of surgeons, orthopedists and medical men the desirability of consolidating interest in the increasing number of fractures on the highways and their proper first-aid and hospital treatment, the committees have gradually increased their scope.

The New England group is particularly fortunate in the educational field. Each regional chairman has a well-organized committee, which holds a fracture symposium of its own at least once a year; the Boston teaching hospitals provide a one-day clinic for the full combined membership of the six regional committees once a year; and the New York, Philadelphia and New England groups hold a two-day clinic alternately in one of the three largest cities each year.

With three meetings a year, the members of these regional groups have an opportunity to keep informed and up to date on all accepted types of fracture treatment. These committees are active in all six states.

AUGUSTUS THORNDIKE, JR., M.D., *Secretary,*
Massachusetts Regional Fracture Committee.
319 Longwood Avenue,
Boston.

"FAITH HEALING"

To the Editor: Your issue of February, 1941, having included an article entitled, "Criminal Aspects of Faith Healing," by I. H. Rubenstein, and an editorial commenting on the article, may I request the publishing of this corrective letter?

Christian Science is not a "faith cure." Christian Science heals through an understanding of spiritual law. Faith is a component part of the healing work of Christian Science, but faith, which rests upon conviction, upon a demonstrable understanding of God's law, is far from a blind, though trusting, hope that prayer will be answered. Mary Baker Eddy writes, in her book, *Miscellaneous Writings*: "Christian Science is not a remedy of faith alone, but combines faith with understanding, through which we may touch the hem of His garment; and know that omnipotence has all power. 'I am the Lord, and there is none else, there is no God beside me'" (p. 97).

References made by the author of this article to decisions of courts in some jurisdictions seem to imply that Christian Science healing has been condemned by the courts. Findings favorable to Christian Science are not mentioned. Furthermore, practically all the decisions cited relate to occurrences of over a generation ago. They were made from the viewpoint of the then understanding of society as to what Christian Science is and what it does. As a rule society does not unanimously accept what appears to be an innovation. This is true in the arts and sciences, and in the practice of medicine.

In our tolerant and enlightened democracy, Christian Science has demonstrated its efficacy by its works. Consequently, a better understanding and recognition of its healing ministry is evidenced by the action of the citizens of our states in providing through legislative enactments that there may be treatment by prayer or spiritual means in the healing of the sick. So it is that whatever may have been the controversies before the courts in earlier times, it is clear that today healing by prayer has legal sanction and approval because the people wish it so.

The author of the article in question is apprehensive lest the "faith healer" will resort to material remedies in connection with his ministrations, that he will make physical diagnoses, prescribe and administer material remedies, and thus violate the medical-practice act. It need only be said that one who adheres strictly and in good faith to the methods of healing in Christian Science will not medically diagnose human ailments, nor will he use or administer material remedies in connection with treatment by prayer or spiritual means, for the simple and obvious reason that in so doing he would not be practicing the religion of Christian Science.

Your editorial expresses concern that those relying on prayer or spiritual means for healing may disregard quarantine and sanitary laws in cases of contagious and communicable disease. Christian Scientists carefully observe such laws and regulations. We have been told by our leader, Mary Baker Eddy, to be law-abiding citizens. She has instructed us to "obey strictly the laws that be" (*Message to The Mother Church for 1901*, p. 34).

Mr. Rubenstein refers to "exploiting faith healing for commercial profit," and makes a distinction between treatment given in an office building and treatment given in the practitioner's own home or that of the patient or in a church edifice. If the "effectual fervent prayer" of a Christian Scientist is beneficial, can it be said that it is harmful or less beneficial if compensation is given therefor? Jesus, when sending forth his disciples under the injunction to preach the gospel and heal the sick, said, "The labourer is worthy of his hire." If the ministry in general in its redemptive work is entitled to compensation, and justly so, can it be said that Christian Scientists who devote their entire time to the practice of a religion that heals the sick, are less worthy? In her book, *The First Church of Christ, Scientist, and Miscellany*, Mrs. Eddy says: "Till Christian Scientists give all their time to spiritual things, live without eating, and obtain their money from a fish's mouth, they must earn it in order to help mankind with it. All systems of religion stand on this basis" (p. 216).

With respect to the point raised by the author relative to "criminal responsibility of parents" who do not supply medical care for their children, because of "a conscientious belief in faith healing," it will appear that the cases he has cited and his approach to the question must be considered and judged from the viewpoint of society at that time. The author refers to "necessary medical care." What is considered "necessary" in one age may not be so considered in another. The experience of mankind has demonstrated that the word "necessary," as applied to the healing of its ills, is not confined to "necessary medical care," but includes treatment by prayer or spiritual means, as countless of its beneficiaries can attest.

Speaking in a decision cited by the author (People v. Cole), regarding the construction of the statute under consideration in that case, Chief Judge Bartlett, of the Court of Appeals of New York, said, "I deny the power of the legislature to make it a crime to treat disease by prayer."

Many legislatures in our country have specifically provided that parents may have for their children the care and treatment of their choice. One notes an ever-increasing tendency in federal and state legislation to safeguard the interests of parent and child in permitting the remedial care of their own selection and in providing that a child is not to be considered as neglected who has "other remedial care."

Christian Scientists rely on prayer or spiritual means for the healing of the sick, without the use of material remedies. Christian Science is not a "faith cure" nor an emotional process, but is a restatement, in modern times, of the primitive Christian healing practiced by Jesus. In her famous textbook, *Science and Health with Key to the Scriptures*, Mrs. Eddy writes: "The physical healing of Christian Science results now, as in Jesus' time, from the operation of divine Principle, before which sin and disease lose their reality in human consciousness and disappear as naturally and as necessarily as darkness gives place to light and sin to reformation" (Pref. xi).

HERBERT W. BECK,
Christian Science Committee on Publication.
107 Falmouth Street,
Boston.

REPORT OF MEETING

NEW ENGLAND SOCIETY OF PHYSICAL MEDICINE

At a regular meeting of the New England Society of Physical Medicine at the Hotel Kenmore on January 22, Dr. Hallowell Davis discussed the "Clinical Significance of the Electroencephalogram."

Dr. Davis believes that the method is valuable for diagnosis but not for treatment. In contrast to the electrocardiogram, the rate is faster and voltage very much less. The latter is one reason for the relatively late discovery, another being the irregularities of rate and amplitude, which were originally considered insignificant. The speaker briefly discussed various methods of placing the electrodes. Slides were then shown of the different types of waves. Normally there may be some variation in the height of the wave, but this is usually constant for each patient. There is a prominence of the ten-cycle rhythm; in the intermediate waves, there is more variation, but there is a stable base line; in abnormal tracings, the rates are grossly irregular, and the waves have characteristic shapes.

A motion picture was then shown demonstrating the maturation of the brain-wave pattern with increasing age. At ten days there are practically no waves; at six months irregularities are characteristic, being slow, of wide amplitude and of random pattern; at five years there is more regularity, some faster components, and the fundamental rhythm appears in runs; at seven years the fundamental rhythm becomes more prominent, is decreased or absent on opening the eyes, and varies with the state of sleep. Finally, the characteristic adult pattern was shown. The individuality of pattern is similar to that of handwriting, but the close resemblance of patterns in identical twins seems to indicate that it is an inborn characteristic. Brain waves are not exclusive with human beings, for similar tracings may be found in animals of very low order.

Dr. Davis discussed conditions that cause a variation in brain waves. The amplitude is decreased most surely by opening the eyes. Arithmetical problems may or may not cause a diminution, depending on how sensitive the patient is about being "put on the spot." When the patient goes to sleep, the waves become larger and slower, manifesting the same depression as other physiologic activities. Oxygen want acts by a similar mechanism, as does a low blood-sugar level, such as that occurring in the insulin treatment of schizophrenia. Alcoholic intoxication causes surprisingly little depression in the deeper stages, and there is a slow return to normal, proportional to the alcoholic content of the blood. It increased intracranial pressure the pattern becomes slow, irregular and disorganized, no localization being possible when the increased pressure is generalized. In such cases multiple tracings are advantageous.

Among conditions that cause an increase in the pattern are convulsions, whether of Metrazol origin or from epilepsy. The possibility that the increased waves during Metrazol treatments may be of muscular origin has been ruled out in experimental animals by the use of curare. In epilepsy there are, besides the characteristic waves during a seizure, the telltale tracings between seizures. In the grand-mal type of epilepsy, there is an increase in amplitude and rate, with some slow components. The petit-mal seizure is usually accompanied by the characteristic spike-and-wave pattern. The psychomotor attack results in variable tracings, with a six-per-second rate. In conclusion, Dr. Davis stated that the electroencephalogram is valuable for localizing intracranial disease, detecting epilepsy and following up epileptic treatment.

The second speaker was Dr. Robert Schwab, who recounted how the number of such studies at the Massachusetts General Hospital had increased from 20 per month in 1937 to 250 at the present. Dr. Schwab stated that, besides the diagnosis of epilepsy and the localization of tumors, the method may be employed for recording other emanations, such as those from the neuromuscular system. The speaker then discussed its use in the localization of tumors. Five hundred electroencephalographic studies have been carried out at the Massachusetts General Hospital, and they are grouped as positive, uncertain and negative for tumor. Of those in the first group, 40 of 45 cases have been verified, and in the third group the results have been approximately 90 per cent correct. This compares favorably with the results obtained with air encephalography, and where both agree the results have been 100 per cent correct. From a practical standpoint, it is well to be aware that the use of electrocautery in the operating room nullifies the electroencephalogram. It was also pointed out that by this method one is unable to differentiate subdural hematoma or brain abscess and tumors.

The third speaker was Mrs. Pauline Davis, who has had considerable experience with this method in mental institutions. She has found that "poor co-operation" may be due to a real inability of the patient to concentrate, as manifested by the slow tracings in such patients. In an attempt to correlate the diagnosis with the brain-wave pattern, Mrs. Davis divided the tracings into three groups according to their form and then looked up the diagnoses of these patients. It was found that the 244 schizoid patients fell into these three groups, and that the type of schizophrenia corresponded well in the majority of cases. The patients in the first group, with normal tracings, were paranoid and usually stable on the ward; the second group revealed dysrhythmic waves, and the patients were catatonic and unpredictable in their behavior; the third group had choppy patterns, and the patients were also catatonic, but stable, although retarded, mute and unresponsive.

Occasionally some underlying disease was found to be responsible for the insanity. In this group, in which the patients show organic damage, Metrazol therapy is probably contraindicated, for many show increased damage after treatment, as recorded by the electroencephalogram. Even in those who show a good temporary response, there is usually some eventual damage, with failure of the brain to return to normal activity following therapy. It seems, therefore, that this is a good method for determining the status of the brain prior to treatment and for following the course of treatment.

During the discussion Dr. Davis stated that the locus of origin for brain waves is well localized in the gray matter despite the physiologic interconnections of various parts of the brain. The pattern in hibernation, it was stated, would probably be slow, as in sleep. It is impossible to state whether this latter phenomenon is due to anoxia, but Dr. Davis believes that this is not the explanation. Refrigeration experiments at the McLean Hospital have been carried out, but it has been found that the extreme shivering interferes too greatly with the results.

In discussing schizophrenics, Dr. John Romano pointed out that slow waves may be found in other problem patients. And although psychologists admit the heterogeneity of schizophrenics, he considers it premature to believe that any correlation of types with brain waves is possible at present.

The so-called "frequency analyzer" may have some advantages, but it cannot record wave form, which is so important in epilepsy, for example. In answer to the question how long a record is necessary before epilepsy may be diagnosed or ruled out, it was stated that 90 per cent of positive clinical patients revealed some abnormality within ten minutes, or within three minutes during overventilation. Most of the other 10 per cent reveal characteristic tracings if several tests are carried out on successive days. It was pointed out that about 10 per cent of normal people with abnormal brain-wave patterns have moderately abnormal tracings, whereas none are so markedly pathologic as those among the frankly deranged. It was emphasized that a person who is clinically free of epilepsy may be able to pass on the trait genetically.

In the localization of deep tumors, the results have so far been more uncertain than in the more superficial ones. Differentiation between idiopathic epilepsy and the posttraumatic type may often be made by the generalized irregularities of the former, compared with the focal derangements in the latter. Mrs. Davis pointed out that the electroencephalogram in the depressed manic-depressive patient merely swings in his rare moments of manic activity toward the normal.

NOTICES

ANNOUNCEMENTS

Dr. Bernard Appel announces the removal of his office from 483 Beacon Street, Boston, to 281 Ocean Street, Lynn.

Dr. Louis E. Wolfson announces the reopening of his office at 113 Bay State Road, Boston, for the resumption of his practice.

BOSTON DOCTORS' SYMPHONY ORCHESTRA

The Boston Doctors' Symphony Orchestra will rehearse under Alexander Thiede, formerly concertmaster of the Cleveland Symphony Orchestra, every Thursday at 8:30 p.m. Those interested in becoming members should communicate with Dr. Julius Loman, Pelham Hall Hotel, Brookline (BEA 2430).

SOUTH END MEDICAL CLUB

The next regular meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on Tuesday, April 15, at 12 m. Dr. Richard Chute will speak on "The Present-Day Treatment of Prostatism."

Physicians are cordially invited to attend.

TUFTS CHAPTER OF ALPHA OMEGA ALPHA

The Tufts Chapter of Alpha Omega Alpha will hold its annual lecture at Tufts College Medical School, Room 5, Thursday, April 10, at 4:15 p.m. Dr. Harold D. Chope will speak on "Public Health and National Defense."

All interested are cordially invited to attend.

TUFTS MEDICAL ALUMNI LECTURE

The annual alumni lecture of the Tufts College Medical School will be given at the medical school on Wednesday, April 9, at 4 p.m. Dr. Sara M. Jordan, '21, will speak on "Gastrointestinal Diseases."

Physicians and medical students are cordially invited to attend.

HOSPITAL COUNCIL OF BOSTON

The annual meeting of the Hospital Council of Boston will be held at the Palmer Memorial Hospital, 195 Pilgrim Road, Boston, on Tuesday, April 15, at 12:30 p.m.

Program

Current Legislation. Dr. Henry M. Pollock.
Uniform Hospital Accounting. Mr. Frank E. Wing.
Convalescence and the Nursing Home Information Bureau. Miss Carrie M. Hall, R.N.

Members of the medical profession are cordially invited to attend. The charge for luncheon will be 75 cents. Reservations should be made before April 12 (LIB 8515).

EVANS AUDITORIUM

The first of a series of lectures by Dr. Albert B. Ferguson on "Roentgenology of the Bones and Joints" will be delivered at Evans Auditorium, 78 East Concord Street, Boston, on Monday, April 14, at 7:30 p.m.

The medical profession is invited.

HARVARD MEDICAL SOCIETY

The next meeting of the Harvard Medical Society will be held in the Peter Bent Brigham Hospital amphitheater on Tuesday, April 8, at 8:15 p.m.

Program

Presentation of cases.
Disabilities in Reading and Their Remedying. Professor Walter F. Dearborn, Harvard University.

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Sunday, April 6

Monday, April 7

12:15–1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

Tuesday, April 8

*9–10 a.m. Pancytopenia. Drs. William Dameshek and E. B. Miller. Joseph H. Pratt Diagnostic Hospital.
12:15–1:15 p.m. Clinicoroentgenologic conference. Peter Bent Brigham Hospital amphitheater.
8:15 p.m. Harvard Medical Society. Peter Bent Brigham Hospital amphitheater.

Wednesday, April 9

*9–10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.
*12 m. Clinicopathological conference. Children's Hospital.
4 p.m. Tufts Medical Alumni lecture. Dr. S. M. Jordan. Tufts College Medical School.

Thursday, April 10

*8:30 a.m. Combined clinic of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital, at the Children's Hospital.
*9–10 a.m. The Problem of Vasomotor Rhinitis. Dr. L. R. Weiss. Joseph H. Pratt Diagnostic Hospital.
*4:15 p.m. Public Health and National Defense. Dr. Harold D. Chope. Tufts Chapter of Alpha Omega Alpha. Tufts College Medical School, Room 5.

Friday, April 11

*9–10 a.m. Certain Aspects in the Diagnosis and Treatment of Contagious Diseases. Dr. E. H. Place. Joseph H. Pratt Diagnostic Hospital.

Saturday, April 12

*9–10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*Open to the medical profession.

April 10 — New England Society of Psychiatry. Page 531, issue of March 20.

APRIL 10 — Pentucket Association of Physicians. Page 263, issue of August 15.

APRIL 13 — Free public lecture, Quincy City Hospital. Page 436, issue of March 6.

APRIL 14 — Lecture. Evans Auditorium. Page 624.

APRIL 15 — South End Medical Club. Page 624.

APRIL 15 — Hospital Council of Boston. Page 624.

APRIL 21–25 — American College of Physicians. Page 1065, issue of June 20.

APRIL 25 — Salem Tumor Clinic. Page 579, issue of March 27.

APRIL 28–30 — American Academy of Physical Medicine. Scientific session. Page 579, issue of March 27.

APRIL 30 — Boston Society of Biologists. Page 579, issue of March 27.

MAY 5–9 — American Association of Industrial Physicians and Surgeons and American Industrial Hygiene Association. Page 484, issue of March 13.

MAY 13–16 — National Gastroenterological Association. Hotel Commodore, New York City.

MAY 21, 22 — Massachusetts Medical Society, Boston.

MAY 28–JUNE 2 — American Board of Obstetrics and Gynecology. Page 262, issue of February 6.

MAY 30, 31 — American Heart Association. Hotel Statler, Cleveland.

MAY 30–JUNE 2 — American College of Chest Physicians. Hotel Statler, Cleveland, Ohio.

JUNE 2–6 — American Medical Association. Cleveland, Ohio.

OCTOBER 14–17 — American Public Health Association. Page 579, issue of March 27.

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DISTRICT MEDICAL SOCIETIES

ESSEX SOUTH

MAY 14 — Relation of the Doctor to the Law. Mr. Leland Powers. New Ocean House, Swampscott.

FRANKLIN

MAY 13 — This meeting will be held at 11 a.m. at the Franklin County Hospital, Greenfield.

NORFOLK

MAY 8 — Censors' meeting. Hotel Puritan.

SUFFOLK

APRIL 30 — Page 604, issue of October 10.

MAY 1 — Censors' meeting. Page 261, issue of February 6.

WORCESTER

APRIL 9 — Hahnemann Hospital, Worcester.

Supper at 6:30 p.m. followed by a business meeting and scientific program.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Williams Obstetrics. By Henricus J. Stander, M.D., professor of obstetrics and gynecology, Cornell University Medical College, obstetrician and gynecologist-in-chief, New York Hospital, and director of the Lying-In Hospital, New York City. Eighth edition. 8°, cloth, 1401 pp., with 13 plates and 704 illustrations. New York: D. Appleton-Century Company, Incorporated, 1941. $10.00.

The Care of the Psychiatric Patient in General Hospitals. By Franklin G. Ebaugh, M.D., director, Colorado Psychopathic Hospital, professor of psychiatry, University of Colorado School of Medicine, and director, Division of Psychiatric Education, National Committee for Mental Hygiene, New York City. 8°, cloth, 79 pp. Chicago, Illinois: American Hospital Association, 1940. $1.00.

Age Morphology of Primary Tubercles. By Henry C. Sweany, M.D. medical director of research, Municipal Tuberculosis Sanitarium, Chicago, and research associate, Department of Physiology, University of Chicago. 8°, cloth, 265 pp., with 73 illustrations. Springfield, Illinois: Charles C Thomas, 1941. $5.00.

Manual of Physical Diagnosis: With special consideration of the heart and lungs. By Maurice Lewison, M.D., professor of physical diagnosis, University of Illinois College of Medicine, consulting physician, Cook County Hospital and attending physician, Mount Sinai Hospital, Chicago; and Ellis B. Freilich, M.D., associate professor of medicine, University of Illinois College of Medicine, professor of medicine, Cook County Graduate School of Medicine, attending physician and chief of Tuberculosis Staff, Cook County Hospital, consultant to the Chicago Municipal Tuberculosis Sanitarium, attending physician, University Hospital, and associate attending physician, Mount Sinai Hospital. In collaboration with George C. Coe, M.D., instructor of medicine, University of Illinois College of Medicine, associate physician, Cook County Hospital, and clinical assistant, Mount Sinai Hospital. 8°, cloth, 317 pp., with 75 illustrations. Chicago: The Year Book Publishers, Incorporated, 1941. $3.00.

The Therapy of the Neuroses and Psychoses: A socio-psycho-biologic analysis and resynthesis. By Samuel Henry Kraines, M.D., associate in psychiatry, University of Illinois, College of Medicine, and assistant state alienist, State of Illinois. 8°, cloth, 512 pp. Philadelphia: Lea and Febiger, 1941. $5.50.

Anus — Rectum — Sigmoid Colon: Diagnosis and treatment. By Harry Ellicott Bacon, M.D., clinical professor of proctology, Temple University School of Medicine, associate professor of proctology, Graduate School of Medicine, University of Pennsylvania, visiting proctologist, St. Luke's and Children's Hospital, proctologist, National Stomach Hospital, consultant proctologist, Mercy Hospital, and consultant proctologist, Paul Kimball Hospital, Lakewood, New Jersey. Introduction by W. Wayne Babcock, M.D., professor of surgery, Temple University School of Medicine. Foreword by J. P. Lockhart-Mummery, M.B., B.C. (Cantab.), F.R.C.S. (Eng.), emeritus surgeon, St. Mark's Hospital, London, England. Second edition. 8°, cloth, 857 pp., with 507 illustrations. Philadelphia: J. B. Lippincott Company, 1941. $8.50.

Born that Way. By Earl R. Carlson, M.D. 12°, cloth, 174 pp. New York: The John Day Company, 1941. $1.75.

Electrocardiography in Practice. By Ashton Graybiel, M.D., instructor in medicine, Courses for Graduates, Harvard Medical School, research associate, Fatigue Laboratory, Harvard University, and assistant in medicine, Massachusetts General Hospital; and Paul D. White, M.D., lecturer in medicine, Harvard Medical School, and physician, Massachusetts General Hospital, in charge of the Cardiac Clinics and Laboratory. 8°, cloth, 319 pp., with 272 illustrations. Philadelphia and London: W. B. Saunders Company, 1941. $6.00.

The American College of Physicians: Its first quarter century. By William Gerry Morgan, M.D., LL.D., Sc.D., professor of gastroenterology and emeritus dean, Georgetown University School of Medicine, Washington, D. C. 4°, cloth, 275 pp., with 36 illustrations. Philadelphia: American College of Physicians, 1940. $2.00.

Routine Practices: Medical Service of the Peter Bent Brigham Hospital. Compiled by the members of the Medical Service. 8°, cloth, 145 pp. Boston: Peter Bent Brigham Hospital, 1940. $1.00.

The Medical Clinics of North America. Vol. 24, No. 6, November 1940: Philadelphia Number. With three-year cumulative index, Vol. 22, 23, and 24 (1938, 1939 and 1940). 8°, cloth, 325 pp., with 35 illustrations and 12 tables. Philadelphia and London: W. B. Saunders Company. $2.67.

The Medical Clinics of North America. Vol. 25, No. 1, January, 1941: Chicago Number. 8°, cloth, 302 pp., with 35 illustrations and 11 tables. Philadelphia and London: W. B. Saunders Company, 1941. $2.67.

Textbook for Male Practical Nurses. By Gayle Coltman, R.N. 12°, cloth, 215 pp., with 7 illustrations. New York: The Macmillan Company, 1941. $2.00.

Hospital Formulary and Compendium of Useful Information. Compiled by the University of California. 16°, cloth, 270 pp. Berkeley and Los Angeles: University of California Press, 1941. $2.00.

The Voice Governor: Give it a chance: Correct body mechanics does it. By Ralph M. Harper. 8°, cloth, 142 pp., with 40 illustrations. Boston: E. C. Schirmer Music Company, 1940. $2.00.

BOOK REVIEWS

Surgery of the Hand. By R. M. Handfield-Jones, M.C. M.S., F.R.C.S. 8°, cloth, 140 pp., with 95 illustrations. Baltimore: Williams and Wilkins Company, 1940. $4.50.

This book deals with surgical affections of the hand and discusses their diagnosis and treatment in detail. No new facts are presented, but the old ones are so important as to bear frequent repetition. The author has maintained throughout this work a healthy emphasis on early motion in infections of the hand. There is included a timely chapter on prevention of serious sepsis from minor injuries, and the use of the sulfonamide group is given an important place in the management of sepsis. It is interesting to note that the author recommends passive venous congestion in the treatment of acute lymphangitis —a measure that has been largely abandoned in this country.

This book will serve as a valuable reference for those who are learning about and those who are handling infections of the hand.

Arthritis and Allied Conditions. By Bernard I. Comroe, M.D. 8°, cloth, 752 pp., with 200 illustrations. Philadelphia: Lea and Febiger, 1940. $8.50.

This meaty and profusely illustrated volume is probably the most comprehensive American survey thus far published in book form of the field of the rheumatic diseases. Over 2700 bibliographic references attest the wide scope of the author's review of the literature on these conditions. The illustrations are excellent, although largely chosen from other textbooks and monographs.

The forty-seven chapters not only deal with the pathology, etiology and general therapy of the different types of arthritis, but also describe in useful detail many of the special technics of administration, such as fever therapy, the use of gold salts, massage and exercises. Helpful warnings are given concerning the possible dangers to be escaped and the pitfalls to be avoided in therapy.

The reader is likely to wish at times that the author had been less dispassionate and had expressed in more definite phraseology his personal convictions and recounted his own experiences, as he has for example in his discussion of vaccine therapy. In reference to this much mooted question, the author believes from clinical evidence that vaccine therapy is an "integral part" of the therapy of rheumatoid arthritis, but that an honest answer to the question, "How do vaccines work?", is, "No one knows."

The allied conditions cover a wide field, as the titles of certain chapters suggest, such as "Internal Derangement of Joints," "The Painful Shoulder" and "Painful Feet," as well as the subheadings, "Treatment of Sciatica," "Sprains," "Acute Bone Atrophy" and "Ganglion."

This book can be highly recommended as an excellent and up-to-date reference book that is worthy of the perusal of all internists and orthopedic surgeons dealing with these protean diseases, which are of supreme importance both medically and economically.

Pharmacology and Therapeutics. By Arthur R. Cushny, M.D., LL.D., F.R.S. Twelfth edition, thoroughly revised by C. W. Edmunds, M.D., and J. A. Gunn, M.D., D.Sc., F.R.C.P. 8°, cloth, 852 pp., with 66 illustrations. Philadelphia: Lea and Febiger, 1940. $6.50.

Cushny's standard work on pharmacology and therapeutics has been thoroughly revised since the last edition four years ago. It is interesting to note that 1940 marks the forty-first year since this work first appeared. It has held its own for this long period, and is still a standard textbook. No greater tribute could come to any author than to have his book last through more than two generations of medical students and physicians. The student of today is thus reading the same book in his course of medical education that his father or those of that generation were brought up on.

Applied Pharmacology. By Hugh Alister McGuigan, Ph.D., M.D. 8°, cloth, 914 pp., with 41 illustrations. St. Louis: C. V. Mosby Company, 1940. $9.00.

Although the idea of this book is admirable, some of the execution is disappointing. It contains much useful information, but is not sufficiently complete, pharmacologically or clinically, to be as valuable as it might be. For example, the author fails to discuss the important differences in the disposal of various barbiturates in the body, and many inaccurate statements, such as that Luminal is used at bedtime in cases of epilepsy, are found. The idea and arrangement of the book are excellent. It is particularly valuable in giving the chemistry of some of the drugs.

Subsequent editions—with more careful editing—should make it a very valuable addition to any physician's library.

Principles of Surgical Care, Shock and Other Problems. By Alfred Blalock, M.D. 4°, cloth, 325 pp., with 13 illustrations. St. Louis: C. V. Mosby Company, 1940. $4.50.

In this volume the author discusses the care of the surgical patient. He emphasizes the avoidance of complications but also includes their management when they arise.

The best part of the work is that devoted to shock or peripheral circulatory collapse. The author is an eminent authority in this field and has made many clinical and laboratory contributions. Although his main emphasis has been on the loss of fluid from the blood stream into the extracellular tissue spaces, his summary of the whole problem of shock is as clear and fair a statement as any that has recently appeared. The sections of the book on anesthesia and treatment may be found in any textbook of surgery, but seldom have been better documented.

The book will have an especial appeal to those who follow closely the trends in modern surgery.